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HEXAMETHONIUM* AND APRESOLINE: THEIR EFFECTS ON AMBULATORY HYPERTENSIVE PATIENTS‡

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NEW ORLEANS

This series of cases represents a group of patients with essential hypertension treated with hexamethonium chloride (esomid) and 1-hydrazinophthalazine (apresoline) on an outpatient basis. Our purpose in conducting the study with these drugs was to determine the feasibility of managing cases from the onset on an outpatient basis and to observe the effects of the drug over a reasonable period of time. We readily appreciate the advantages of hospitalizing patients until a supposed safe adequate maintenance dosage has been established, but we also realize the serious obstacles involved in hospitalizing a large group of patients; moreover, it has been shown that so called stabilized maintenance doses of these drugs on hospitalized patients have to be readjusted when these individuals return to their normal routine of life. Because of the rapidity of onset of hypotensive reactions in individuals on fixed doses of these drugs and because of the unreliability of patients attempting to correlate their own blood pressure determinations with changes in dosage, we do not feel that any variation in dosage should be determined by the patient himself on the basis of his taking his own blood pressure. We feel very strongly concerning the advisability of thoroughly familiarizing each patient with the hazards of the drug, the important symptoms and signs of an impending hypotensive reaction, and what procedure to follow when these impending symptoms present themselves. However, reactions may occur in spite of all preventive measures.

Paton and Zaimis[1] introduced a series of polymethylene bistrimethylammonium compounds of which hexamethonium (C_6) compounds are derived. The mode of action of hexamethonium in lowering of blood pressure is in the production of a blockade of autonomic ganglia. 1-hydrazinophthalazine (apresoline) on the other hand acts at various levels on the brain and on the peripheral arterioles. It is also believed that apresoline has the effect of neutralizing humeral pressor substances.[2] One important action attributed to apresoline is that blood flow through the kidneys with and without renal damage is increased, although glomerular filtration is not.[3]

We have followed the generally accepted method of administering these drugs, namely, by giving small initial doses of 250 mg. of hexamethonium every twelve hours in each case. Further increases in dosage and the combination of hexamethonium and apresoline were determined on an individual

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basis, depending on the severity and persistence of reactions, cooperation of the patient, and response of the hypertension. All patients, with the exception of two who discontinued the drug after the first few days, received a combination form of therapy. The average dose for hexamethonium was 500 mg. and 750 mg. alternating at six hour intervals; the average dose of apresoline was 50 mg. at six hour intervals. A few patients in this group were able to tolerate as much as 3 grams of hexamethonium and 400 mg. of apresoline in a twenty-four hour period, the dosage schedule being 750 mg. of hexamethonium and 100 mg. of apresoline every six hours.

TABLE 1
TOTAL PATIENTS—30*

Color	White 13	Colored 17
Sex	Male 9	Female 21
Age	Range 30-60 yrs.	Avg. age 44.7 yrs.

*These patients had been followed previously—some for years.

We have used other drugs and found them wanting — phenobarbital, dihydrogenated alkaloids of ergot, veratrum viride preparations.

TABLE 2
AVERAGE PRETREATMENT BLOOD PRESSURE LEVELS

White	207 mmHg - Systolic
	117 mmHg - Diastolic
Colored	200 mmHg - Systolic
	125 mmHg - Diastolic

TABLE 3
INITIAL RESPONSE—COLORED PATIENTS

	None	Not Significant	Significant
Number of Colored Patients			
17	23.5%	17.7%	58.8%
MAINTAINED RESPONSE	None	Not Significant	Significant
*Number of Colored Patients			
14	71.4%	21.40%	7.2%

*1 patient was not followed for a sufficient length of time. 2 patients refused the drugs after a significant initial response.

TABLE 4
INITIAL RESPONSE—WHITE PATIENTS

	None	Not Significant	Significant
Number of White Patients			
13	7.7%	7.7%	84.6%
MAINTAINED RESPONSE	None	Not Significant	Significant
*Number of White Patients			
10	20%	70%	10%

*3 patients refused the drugs after significant initial responses.

TABLE 5
OVER-ALL RESULTS

Initial Response			Total Patients 30
None	Not Significant	Significant	
16.6%	13.3%	70.1%	
Maintained Response			Total Patients 24
None	Not Significant	Significant	
50%	41.6%	8. 4%	

Reports from medical literature indicate varied responses to these drugs over long term periods of treatment. Enthusiastic reports by Schroeder[2] using a combination form of therapy with hexamethonium and apresoline, and by Moyer[3] using apresoline alone, have added impetus to the accounts of beneficial results obtained in treating hypertension. It is true that these authors used larger doses of apresoline than our group of patients were able to tolerate. On the other hand J. D. Blainey[4] reporting on a group of 34 patients with severe hypertension using hexamethonium in dosage varying from 2 to 6 grams a day reported that all patients after a nine month period showed a return of blood pressure to pretreatment levels; however, during this period all patients showed some degree of hypotensive effect. M. A. Khan[5] reported similar results, using apresoline alone in doses as high as 1200 mg. daily, and in combination with hexamethonium, the dosages being 450 mg. of apresoline and 2250 mg. of hexamethonium daily.

TOXIC EFFECTS

Five patients or 16.6 per cent of the group of 30 patients refused to take the drugs after significant initial responses. This was done in spite of reassurance that the symp-

toms might only be of temporary duration. Unpleasant reactions that precipitated voluntary discontinuance of the drug consisted predominantly of postural dizziness, blurring of vision, weakness and headache. Constipation was a minor complaint. Twenty-four, or 80 per cent of the total of 30 patients had some side reactions, usually during the first few weeks of therapy. Two patients, or 6.6 per cent of the group, had one or more syncopal attacks during the course of treatment—and in both cases the attacks occurred well along during the course of therapy—six weeks after beginning treatment.

CONCLUSION

Our experience with drugs used in the therapy of hypertension leaves us with no doubt that both hexamethonium and apresoline are very potent hypotensive agents. Of the two hexamethonium is the more potent. Both are effective in the majority of cases in producing an initial fall in blood pressure. It is impossible, however, to predict in which patients there will be a hypotensive effect, and it is likewise not possible to determine the duration of the efficacy of these drugs on a long term basis when a hypotensive effect is obtained.

While we are very much encouraged by the hypotensive effects of these drugs, there still remains much to be desired as regards their fulfilling the requirements of an ideal drug for the therapy of essential hypertension. The rather significant fluctuation in blood pressure of patients on these drugs, the severe symptomatology associated with hypotensive levels or a rapid fall in blood pressure, the failure of these drugs to maintain a sustained relative hypotensive effect on a significant number of patients on a normal every day routine, and most important the failure of these drugs to continue to exert their effects over a reasonably long period of time—are some of the obstacles that must be surmounted in order to approach the goal of a better therapeutic regimen for the hypertensive patient.

It is our belief that hypertensive patients can be treated with these drugs on an ambulatory basis with the understanding that these individuals are thoroughly informed regarding side effects and the symptoms of an impending severe hypotensive episode.

REFERENCES

1. Paton, W. D. and Zaimis, E. J.: Clinical potentialities of certain bisquaternary salts causing neuromuscular and ganglionic block, Nature 162:810 (Nov. 20) 1948.

2. Schroeder, H. A.: The effect of 1-hydrazinophthalazine and hexamethonium on hypertension, J. Lab. & Clin. Med. 38:949, 1951.

3. Moyer, John H.: Hydralazine (apresoline) hydrochloride, Arch. Int. Med., 91:419 (April) 1953.

4. Blainey, J. D.: Hexamethonium compounds in the treatment of hypertension, Lancet 1:993, 1952.

5. Khan, M. A.: Effect of hydralazine in hypertension, British M. J. (Jan. 3) 1953.

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THE ROLE OF POTASSIUM IN DIABETIC ACIDOSIS*

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The elucidation of the role of potassium in diabetic acidosis on a clinical level is a relatively recent development which has served to pinpoint a clinical dictum which has been well known and regularly applied for many years—feed them early, particularly with tomato juice, orange juice, bouillon or other meat extracts, thus supplying fluids and "other factors." With greater knowledge, one of these "other factors" of considerable importance has been found to be potassium, thus furthering our understanding of the pathogenesis of previously vaguely understood cases of resistance to therapy. Let me emphasize that this is not the only factor responsible for these recalcitrant cases. Knowledge of the vital role of potassium in these patients only serves to reduce their number.

Gamble's succinct diagrams[1] will serve to define the chemical anatomy of our ion: (Figure 1). Here we see the marked difference in the concentrations of intracellular and extracellular potassium on either side of a semipermeable membrane which, on the basis of the physical characteristics alone of the cell membrane, would be expected to result in an equilibrium at approximately equal concentrations. This marked

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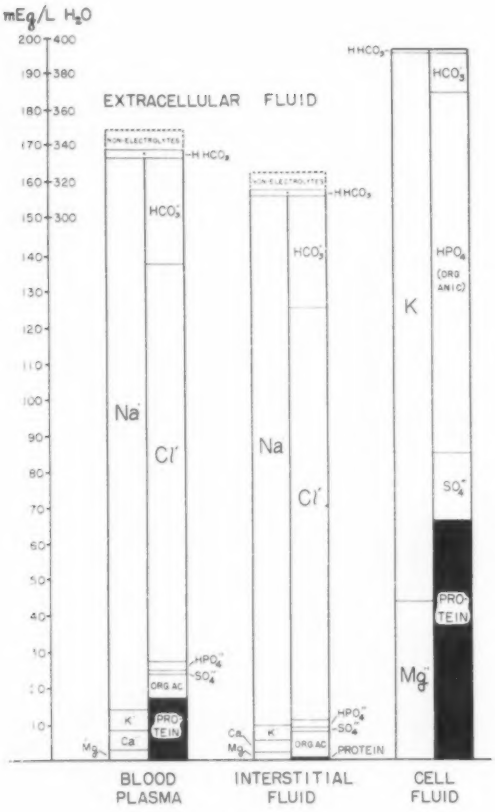

Figure 1

shift in the point at which the equilibrium is maintained is attributed to the "vital" function of the cell membrane, which implies a living cell.[2] As will be seen later, changes in either direction of the concentration of the extracellular potassium, which represents a very small fraction of the total body potassium, will produce profound changes and even death in the type of cases under consideration.

The following simplified diagrams (Figure 2), will permit a more rapid review of the more important factors involved in maintaining the concentration of the extracellular or serum potassium; the capillary membrane, acting only as a semipermeable membrane, not being important in our consideration of potassium, and therefore, not being included in the diagrams. In the normal individual in health, the concentration of extracellular potassium is maintained by

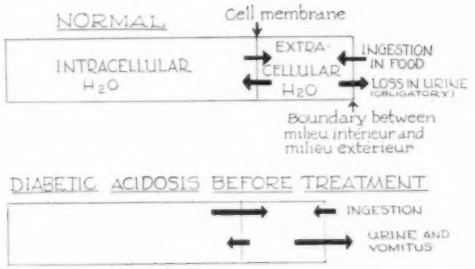

Figure 2

the equilibrium at the cell membrane and the balance between the ingestion and urinary loss of potassium.

With the development of diabetic acidosis, potassium is lost in increasing amounts by the urinary route[3] (until and if progression occurs to shock and oliguria), and frequently vomiting occurs with its further loss of potassium (which is about three times as concentrated in gastric juice as in the serum[4, 5]). The movement of potassium through the extracellular fluid volume is such as to maintain a normal or elevated serum potassium concentration.[6] But the administration of insulin (Figure 3)

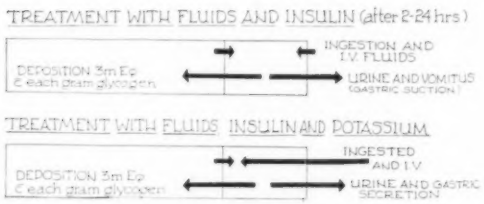
TREATMENT WITH FLUIDS AND INSULIN (after 2-24 hrs.)
INGESTION AND I.V. FLUIDS
DEPOSITION 3m Eq. / each gram glycogen
URINE AND VOMITUS (GASTRIC SUCTION)
TREATMENT WITH FLUIDS INSULIN AND POTASSIUM
INGESTED AND I.V.
DEPOSITION 3m Eq. / each gram glycogen
URINE AND GASTRIC SECRETION

Figure 3

markedly changes the direction of the shift of potassium across the cell membrane, since animal experiments have indicated that approximately three millequivalents of potassium must be shifted into the cells for each gram of glycogen deposited,[7-9] a toll which could, and does, rapidly (within two to twenty-four hours) reduce the serum potassium to levels which can be consistently demonstrated to be low by quantitative determination, and are frequently clinically demonstrable by the following, in order of appearance (Figure 4).

1. Electrocardiographic changes.
   a. Lengthened QT interval, being pri-

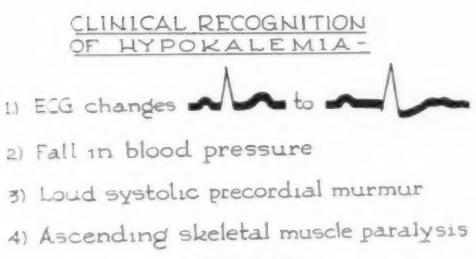

Figure 4

marily prolonged by a low, broad, frequently notched T wave.

b. Depressed ST segments.

2. Fall in blood pressure, particularly diastolic, but eventually systolic also, these readings being a reversal of the direction of change of the blood pressures recorded as the frequently associated initial shock picture is corrected in the first several hours of treatment.
3. Loud systolic precordial murmur.
4. Ascending skeletal muscle paralysis, ranging from general weakness only (most frequent), to demonstrable flaccidity involving first the extremities, then the trunk, and finally the diaphragm and intercostal muscles of respiration, producing the typical fish-mouth gasping for breath because of the sole reliance on the accessory muscles of respiration in the neck. However, not infrequently, isolated and relatively small muscle groups, as of the eye, are involved.

Usually we can start feeding our patients in two to twelve hours and furnish enough potassium to satisfy the metabolic needs of glycogen deposition. (Figure 3). If the usual feedings are not sufficient to prevent the development of evidence of hypokalemia, or lowered serum potassium, then (Figure 5) 2 grams of potassium chloride or citrate may be given by mouth every thirty minutes until 8 to 18 grams are given. However, gastric dilatation and persistent nausea and vomiting only too frequently make this route impractical, and we must resort to the subcutaneous or intravenous route. At this point let me emphasize that a good

TREATMENT of HYPOKALEMIA
I ORAL
A) Soft diet containing foods rich in potassium.
B) 2 gm. KCl or citrate every 30 mins. until 8-18 gms. are given.
II. HYPODERMOCYLSIS
A) Most satisfactory
B) Isotonic (1.14%) solution of KCl or diluted with equal parts of physiological saline.
C) 30 c.c. of 22.3% KCl (2.23 gms. or 30m Eq/10c.c.) added to a liter of parenteral fluid.
D) Do not use hyaluronidase.
E) ECG before and after each 500 c.c.

Figure 5

output of urine should be obtained before the administration of potassium is undertaken, with certain exceptions which need not be entered into in a presentation of this brevity.

Administration of potassium by hypodermoclysis is most satisfactory from the point of view of ease and safety. An isotonic (1.14 per cent) solution of potassium chloride can be used as such, or preferably diluted with equal parts of physiological saline,[10] as reported from other institutions, but at Touro Infirmary a stock solution of 22.3 per cent potassium chloride (2.23 grams or 30 millequivalents per 10 cc.) or of buffered potassium phosphate (5 cc. of 13.6 per cent potassium acid phosphate and 5 cc. of 43.5 per cent potassium basic phosphate constituting a mixture also containing 30 millequivalents of potassium per 10 cc.) is used, about 30 cc. being added to a liter of whatever parenteral fluid is being administered. If hyaluronidase is not used, it is generally safe to check the electrocardiogram after every 500 cc., thus insuring only a return to a normal QT interval and T wave configuration, and not a swing to the opposite extreme of evidence of hyperkalemia, with the following sequence of changes in order of appearance. (Figure 6): A shortened QT interval and tall, peaked T wave, then a broadening of the QRS complex, marked primarily by the appearance of, or broadening of a previously present S-wave, and the prolongation of the PR to the point of heart block, and lastly the sine

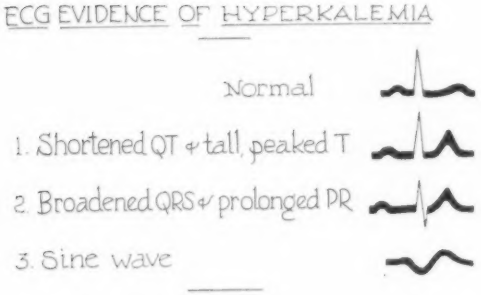

Figure 6

wave just prior to death. Without electrocardiographic control we are interested in administering only enough potassium to correct the blood pressure changes, precordial murmur, and skeletal muscle symptoms previously described.

The route of administration which is indicated in patients with evidence of marked hypokalemia (as when ascending paralysis, and particularly "fish-mouth" type of respiration, have developed), is the intravenous one (Figure 7), but this requires the

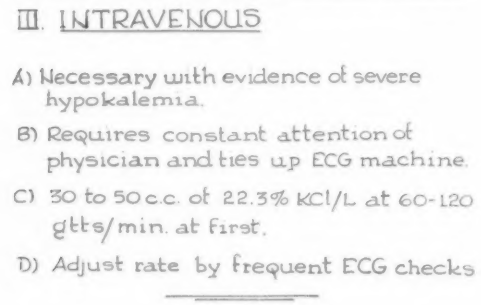
TREATMENT of HYPOKALEMIA (cont'd)
III. INTRAVENOUS
A) Necessary with evidence of severe hypokalemia.
B) Requires constant attention of physician and ties up ECG machine.
C) 30 to 50 c.c. of 22.3% KCl/L at 60-120 gtts/min. at first.
D) Adjust rate by frequent ECG checks

Figure 7

practically constant attendance of a physician with a direct writing electrocardiograph machine for frequent checks of the effects of the serum potassium on the electrocardiogram. For it must be remembered that the transfer of potassium from the extracellular to the intracellular fluid volume is a function of a viable cell membrane, and the time factor is an important consideration—administration of potassium more rapidly than it can be cleared from the extracellular fluid volume results in toxic concentrations which can, and have, resulted in death of the patient in cardiac standstill or ventricular fibrillation. Unfortunately, the "clearance rate" is not predictable from patient to patient, or always in the same patient, so that only approximate rates of administration can be initiated, and control must be exercised by the previously listed criteria. We add from 30 to 50 cc. of our 22.3 per cent potassium chloride solution to a liter of whatever infusion other considerations in the particular patient may indicate, and start with a rate of administration of about 60 to 120 drops per minute, subsequent adjustments being based on the electrocardiographic changes checked at first at five minute intervals, and, when the electrocardiogram has improved to approximately normal, decreasing the rate of administration by about one-third to one-half, and checking further until a rate of administration is determined which maintains a stable and relatively normal electrocardiogram, after which the interval between electrocardiographic checks is gradually increased and the potassium administration is changed to the oral or clysis routes. Usually after twenty-four to forty-eight hours the patient is eating enough to permit adequate control with one or two electrocardiograms per day for a few more days.

CASE REPORT

In August, 1950, a 12 year old girl, a known diabetic since 4 years of age, was brought into the hospital at 9 A. M. in a diabetic coma, responding only to painful stimuli. In addition to the marked dehydration expected, it was also noted that her blood pressure was about 100/60, and reflexes were present in all extremities. Intensive fluid, sodium chloride, and insulin therapy was instituted. However, diuresis progressed at such a rate that after four hours the patient appeared almost as dehydrated as when first seen, despite the fact that she responded somewhat to questions and moved about in bed so as to appear improved clinically. About 2 P. M., after five hours of therapy, it was noted that the patient was moving about less, seemed to have lapsed into coma again, and that the diastolic blood pressure was down to zero. About 3 P. M. reflexes were not obtainable, and a loud systolic precordial murmur was heard for the first time. About 4 P. M. a gasping "fish-mouth" type of respiration was noted, and the patient appeared moribund. Institution of intravenous potassium chloride therapy raised the diastolic blood pressure to her normal, eliminated the systolic precordial murmur, and produced a return of extremity re-

flexes and more normal respiration in thirty minutes to one hour. Although electrocardiographic corroboration of the various stages in the above clinical pictures was obtained, it can be seen that there was a wealth of clinical signs upon which diagnosis and therapy could be based.

SUMMARY

In summary let me emphasize the following points:

1. The role of potassium in diabetic acidosis has been established on a clinical and working basis so that diagnosis and treatment can be accomplished at the bedside by signs and symptoms in a given context.

2. Because of the inevitable physiological concomitants of this process, potassium can and should be administered orally or parenterally about four to six hours after therapy has been instituted, if adequate diuresis has been obtained.

3. The intravenous administration of potassium is dangerous. Those who are not familiar with the possible complications and who do not have adequate control facilities had best never apply this route for the administration of large amounts of potassium in a short period of time.

REFERENCES

1. Gamble, J. L.: Chemical Anatomy, Physiology and Pathology of Extracellular Fluid, 1942.

2. Neubauer, R. A., and Frelick, R. W.: Spontaneous hyperpotassemia as a cause of death in diabetic acidosis, Am. Heart J.: 40:793, 1950.

3. Atchley, D. W., et als: On diabetic acidosis: detailed study of electrolyte balance following the withdrawal and re-establishment of insulin therapy, J. Clin. Invest. 12:297, 1933.

4. Austin, J. H. and Gammon, G. D.: Gastric secretion after histamine: Sodium and potassium content and pepsin estimation, J. Clin. Invest., 10:287, 1931.

5. Frenkel, M., Groen, J., and Willebrands, A. F.: Low serum potassium level during recovery from diabetic coma, Arch. Int. Med., 80:728, 1947.

6. Nadler, C. S., Bellett, S., Reinhold, J. G., Lanning, M.: Alterations in the serum potassium and their relation to certain constituents of the blood in diabetic acidosis, Am. J. Med. Sci., 218:308, 1949.

7. Fenn, W. O.: The deposition of potassium and phosphate with glycogen in rat livers, J. Biol. Chem., 128:297, 1939.

8. Boyer, P. D., Lardy, H. A., and Phillips, P. H.: The role of potassium in muscle phosphorylations, J. Biol. Chem., 146:673, 1942.

9. Aitken, R. S., Allott, E. N., Castleden, L. I. M., and Walker, Mary: Observations on a case of familial periodic paralysis, Clin. Science, 3:47, 1937.

10. Nadler, C. S., Ballet, S. Gazes, P. C., and Steiger, W. A.: Administration of potassium to patients with prolonged vomiting and diabetic acidosis, J. Lab. & Clin. Med., 35:842, 1950.

DIABETES IN CHILDHOOD*

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Diabetes occupies a unique position in the field of medicine in that it is one of the very few disorders that may have its onset at any age—from the toddling babe to the octogenarian. Though the abnormal physiology is basically the same regardless of age, the clinical picture and the response to therapy vary so greatly in the various decades that it is necessary to give special consideration to age groups, more particularly to children.

I know of no case on record of a child born with diabetes, yet there are reported cases of onset at nine weeks and thereafter. It is difficult to estimate the number of juvenile diabetics in this country. The National Health Survey revealed that under age 15, one child in 2500 has diabetes. Joslin suspects that there are 60,000 diabetics now living whose disease began in childhood—this would seem conservative.

Sir William Osler in his textbook of 1892 stated: "In children the disease (diabetes) is rapidly progressive, and may prove fatal in a few days." This was literally true before the days of insulin, and is still true unless informed parents recognize early symptoms and astute doctors make an early diagnosis and institute therapy immediately. Childhood diabetes proceeds invariably to acidosis, coma, and death within from three to twelve months unless treated with insulin.

ONSET

The onset of diabetes in children is most often relatively abrupt and dramatic. Though varying in detail, a typical case will run something like this: The child will probably be sturdy, healthy, and of normal weight, and parents will likely as not be nondiabetic. There may have been an acute illness in the immediate past. Almost simultaneously there will develop the classic quartet of symptoms: (1) an increase in appetite (though this may be negligible),

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accompanied by (2) a paradoxical weight loss that, at its height, may amount to a pound a day, (3) an unquenchable thirst that may result in the consumption of 3 to 4 gallons of water a day and a resultant (4) polyuria. These symptoms tend to progress. The child appears literally to spend his time going from ice box to water fountain to bathroom! If these symptoms are not interrupted within one to two to three weeks by proper treatment, there will usually develop apathy, irritability and drowsiness.

Most alert parents will bring the child for examination during this time. The patient will present an ill appearance—has become underweight, lifeless and dehydrated. The urine will invariably show strong glycosuria and ketonuria, and a confirmatory blood sugar, which may be taken at any time during the day, will be high, usually in excess of 300 mgm.%. The child is in mild acidosis and institution of treatment at this time will avoid dread diabetic coma which, in due time, would inevitably ensue. Therefore, whereas in adults the onset of clinical diabetes may be ironically insidious manifesting itself in terms of months and years, in children the problem is one of days or weeks, though one child reported by Colwell, age 12, had an onset of four years. Often the diagnosis may present difficulties in adults, requiring a glucose tolerance test for confirmation; rarely is such true of children. The diagnosis may be made in 99 per cent of cases from the simple urine specimen. As a matter of fact, when the diagnosis is in doubt in a child, diabetes is usually not present. However, renal glycosuria is occasionally seen in which there is glycosuria with normal blood sugars. In these cases galactosuria should be ruled out by fermentation studies. Obviously, there are many variables in the typical case described above. In general, the younger the child the more rapid and vicious the onset. However, regardless of age, the facts remain the same—the difference being one of timing.

I know little of true infantile diabetes, this discussion being that of children from two years and on. Farrell, Hand, and Newcomb of Children's Memorial Hospital in Chicago have reported a series of 7 cases of diabetes in infants with sudden onset involving chills, fever, stupor, nuchal rigidity, rales in the chest, and other evidences of an acute febrile illness. Diagnosis in each instance was unsuspected and the mortality was high in spite of treatment.

The child whom you have just found to have diabetes is literally dying. There are methods at your disposal which will save his life but it will take a great deal of your time, your patience and your knowledge. This will prove to be a relatively unremunerative case. For the next few days you will spend much time in altering this vicious sequence of events and in orientating the confused and disturbed parents, not to mention the tedious hours of instruction as you literally become the life-long guardian of this child's physical and emotional development. If you do not wish to undertake this obligation, refer the child to someone who does.

In the younger child the parents are obligated to learn the facts of control; the child, however, being taught to do urine testing and even to give his own insulin as early as possible. A diabetic child is reared as all children should be. They must not be treated as afflicted children. They must be taught at an early date self discipline and self reliance. They tend to develop a sense of responsibility and to mature earlier than the average child. When well controlled, they are a healthy lot and tend to be above the average in general intelligence. The petted, spoiled, overprotected diabetic child will eventually destroy himself as adulthood tends to separate him from parental protection. Actually, however, the diabetic child, if given half a chance, adapts himself amazingly well to his disorder much to the surprise of all concerned.

Eack, however, to the clinical picture of the just diagnosed diabetic child and a few suggestions regarding control measures to be employed. It is essential that the patient be hospitalized immediately upon diagnosis. The period of control can be divided into

three rather definite periods, lasting approximately six weeks:

THREE PERIODS OF CONTROL

1. Establishment of diet and insulin to overcome glycosuria and ketonuria. Rapid relief from symptoms will be noted and weight gain commence—takes about *one week.*
2. Period of metabolic recovery. The child will continue to improve subjectively and objectively. There will develop a progressive improvement in tolerance for glucose, and insulin will be judiciously reduced from its high peak. Hypoglycemia must be avoided. Lasts *two to three weeks.*
3. Period of stabilization—insulin requirement becomes relatively constant—*one to two weeks.*

This child, if not vomiting, should be placed on an appropriate diet for his age at the onset. A child's food needs are relatively great and though there are charts available with calculated diets for various age groups, the following rules are practical and helpful:

FOOD REQUIREMENTS FOR CHILDREN

1. Total calories per day will average 1000 plus 100 for each year of age.
2. Protein requirement should average approximately 2 grams per pound per day or about 20 per cent of total calories (50-70 grams).
3. Carbohydrate intake should constitute approximately 40 per cent of the total calories. (Average 140-200 grams).
4. Fats are added in amount to complete caloric need.

There is a certain trial and error factor in the regulation of a child's diet. Once the basic diet is established, changes can be made depending on appetite and weight response. It is likely that when the child's appetite levels off after four to six weeks, the diet may have to be reduced. Further, inasmuch as a formal diet is desirable at all times, a growing child's diet should be recalculated yearly. The measured diet is satisfactory though weighing food at the onset is good training for both mother and patient.

There are several different opinions as to the best insulin for children and as to the distribution of the food. I have a strong feeling that Type NPH insulin gives by far the best coverage in children and, if used, the food should be distributed with this insulin in mind. Suggested distributions are:

DISTRIBUTION OF THE DIABETIC DIET FOR CHILDREN

Breakfast	Lunch	Snack	Supper	Bedtime Snack
1/5	2/5	Yes	2/5	Yes
		OR		
1/3	1/3	Yes	1/3	Yes

The snacks should be protein and or carbohydrate foods of about protein-5 grams, carbohydrate-15 grams value.

INSTITUTION OF INSULIN THERAPY

When the control is first instituted, it is best to use unmodified insulin "on demand" for the first few days. An appropriate plan would be to collect urine specimens every four hours day and night and give regular insulin as follows:

If urine is 4 plus give 16 units
If urine is 3 plus give 12 units
If urine is 2 plus give 8 units
If urine is 1 plus give 4 units

As clearing of sugar appears, the night specimens may be gradually omitted. One is always surprised at how much insulin a child will need daily at the onset—80 units plus or minus not being unusual, the need decreasing by the day. The extreme sensitivity of infants to insulin must be remembered, however, their dosage of insulin being calculated in tenths of a unit. As the insulin dosage appears to level off, one should switch to Type NPH insulin, giving a total morning dose of approximately three-fourths the total regular insulin of the last day. From this point on it is a matter of watching urine specimens before each meal and bedtime and altering insulin as judgment dictates. It is unwise to supplement with regular insulin except in the morning and even then it is risky. Children react badly to venepuncture and blood sugars are of little value until the urine specimens are relatively clear. The micro-method of calculating blood sugars is better in children.

Usually a child's initial hospitalization will last seven to fourteen days, the first stage of control having been completed. Thereafter, at home the mother will be obligated to lower insulin gradually, depending on q.i.d. urine specimens. In fact, one must anticipate the expected increase in tolerance and lower the doses, perhaps daily, *before* the specimens become all negative. Most children may be well regulated on one morning dose of NPH insulin; awkward insulin schedules are to be avoided. The daily insulin dose will vary with the child, some 5 and 6 year olds doing well on 6 to 12 units per day. It has been said that, on an average, a child when well controlled will require an insulin dosage that may be calculated by multiplying his age by 3. However, there are no dependable rules and the final maintenance dose will have to be determined in each individual case.

It is well to mention at this point that hypoglycemia is to be carefully avoided in children. The episode is sudden and dramatic in onset and recent observations indicate that irreparable brain damage may occur resulting in permanent mental retardation, epilepsy, and spastic paraplegia. During the period of control it is the doctor's responsibility not to overdo the insulin; later the child must be taught the symptoms of early insulin shock and should carry lump sugar to use in emergencies. In the event that coma should ensue as a result of hypoglycemia, 0.5 ml. of epinephrine should be given immediately and followed by a conservative amount of glucose intravenously.

During the initial control period a search should be made for infection and if even suspected, daily penicillin is indicated. Throughout the child's life all infections, either localized or systemic, should be considered emergencies as these are the most common precipitating causes of diabetic coma in children. During infection, regardless of appetite, insulin need almost invariably increases and this fact, together with the uncertainty of constant food intake, suggests that it is a good plan to discontinue modified insulin and return temporarily to "insulin on demand" as indicated every four hours. Certainly the ketonuria should be carefully watched.

There are several general considerations worth remembering. A child's control should be maintained as close to normal as possible yet it is unsafe for him to have a constantly negative urine specimen; to spill sugar once or twice a day is acceptable. Exercise tends to upset the balance toward hypoglycemia and requires extra food. On the other hand, an emotionally disturbed child may begin to spill sugar and ketone bodies and may require temporary increase in insulin. There is no place in the life of a child diabetic for the so-called "free diet" advocated by those who believe hyperglycemia is a relatively unimportant feature of the disease. We cannot, however, completely disregard the honest concept of Guest that moderate hyperglycemia is acceptable and does not hasten complications. It is to be hoped that this controversy may be clarified in time. If we are to believe Joslin's thought that perfect control (impossible) will prevent complications, and on the other hand are to avoid hypoglycemia, then literally a balanced child diabetic is a bit like a tight rope walker!

In due time the diabetic child will develop a remarkable degree of balance with insulin changes required infrequently. However, it is to be remembered that diabetes is not a static state and one must watch for sudden unexplainable changes in tolerance and alter insulin early. Diabetes, previously easy to handle, will become erratic in its behavior at puberty and require special attention involving insulin increases. Teen-age diabetes is perhaps the most difficult of all to handle both because of intrinsic changes in the diabetic state and because the youngster is in a period of emotional unrest and social development with oft times a resultant resentment toward the self discipline imposed by his disorder plus some self consciousness. The instinct to be "one of the gang" is often greater than that of self preservation and he is likely to

break "training rules." Then, he is badly in need of counseling and encouragement.

EMERGENCY TREATMENT

Most children are at least mildly acidotic by the time the initial diagnosis of diabetes is made. The symptoms of such will respond promptly to therapy as before outlined. Unfortunately, however, some drift into the entirely preventable complication of profound acidosis resulting in coma. Treatment is indicated on an emergency level to preserve life. Such treatment follows the basic principles outlined for adults with a few reservations. An outline of recommended procedure follows:

1. Hospitalization is mandatory.
2. A catheter, if indicated, is inserted and left in place and urine specimen collected by the drop method every two hours.
3. If the patient has received no insulin in six to twelve hours, he is given I unit of insulin per pound of body weight. One half of this amount may be given intravenously if the patient is in shock.
4. Intravenous physiological saline is instituted immediately and given as rapidly as tolerated. After one to two hours, 5 per cent glucose in saline is substituted and administration is reduced to 400-800 ml. per hour.
5. Depending on the condition of the patient, regular insulin is given every three to four hours in doses of 1 unit for each 3 to 4 grams of glucose administered or "on demand" as follows:

+ + + +	16 units
+ + +	12 units
+ +	8 units
+	4 units

6. If food is not taken within six to eight hours, 1 to 2 grams of potassium chloride may be added to the intravenous mixture.
7. When food is tolerated, the amount is dictated only by the patient's appetite and regular insulin is continued as above at four and then six hour intervals. In due time an appropriate diet is prescribed and NPH insulin started as a single morning dose.

Blood sugar determinations are not particularly helpful, the urine tests for both sugar and ketone bodies being a dependable guide for insulin administrations and evaluation of progress. Actually the *p*H of the blood is a more critical index and its use as a guide is becoming more popular. The insulin requirement will remain relatively high for some period of time after an episode of acidosis. Some recommend the use of alkaline therapy if the CO_2 combining power is below 20 volume per cent (using either sodium bicarbonate or Hartmann's solution.) In my experience these have been unnecessary.

LONG TERM CONTROL

I once erroneously thought a diabetic on a reasonable amount of insulin, though poorly controlled, would not go into diabetic coma. However, I have seen innumerable examples of such happening. Contributing circumstances are long term poor control with inadequate insulin onto which is superimposed either infection, neglect to take insulin a day or two, or an emotional upset. The need for all diabetic children to have urine checked 4 times a day for sugar and once a day for ketone bodies is again emphasized.

Fortunately, today, children do not die in diabetic coma, thanks to Banting and Best, and our attention is directed toward the long-term followup of the diabetic child. What are his prospects and what does he have to look forward to? Certainly the outlook is encouraging. Much credit is due the Joslin group for teaching throughout the years the value of close control of the diabetic in an effort to minimize complications, but only recently did I hear Marble state that it is their feeling that optimum control may even *prevent* complications. Unfortunately, this is probably an overly optimistic statement. Obviously, no one has been on insulin over thirty years and that number is unknown. It will take thirty more years to evaluate th life expectancy of children. It is difficult or impossible to maintain "perfect control" throughout a child's years of growth and development. I know many young people who have been on insulin twenty to thirty years. Some show

retinal changes and albuminuria and others show no demonstrable damage. These latter have had long-term favorable control.

I am thinking of one young man of 20, a diabetic for twelve years, now stunted in growth, with a fatty liver, retinal changes and kidney damage. He illustrates the tragedies of childhood diabetes—the loss of a mother at age 12, little home life or moral encouragement thereafter and, hence, atrocious control throughout the years. I can recall a girl, now age 30, a diabetic since age 3, in an excellent state of health; her medical care and self management have been of the best.

Jackson of Iowa and Priscilla White of Boston have each analyzed the records of an impressive number of diabetic children and find that there is a strong evidence to indicate that a high level of control is essential to survival and protection. Graphic Associates for Public Affairs Committee estimated life expectancy of a 10 year old diabetic as thirty-two more years ten years ago, and as forty-five more years today. It is to be hoped that expectancy may be extended in the future.

The child's amazing adaptability to the diabetic regime has been mentioned. It is essential, furthermore, that he be a member of a well adjusted home; that he receive consideration but not over solicitude; and that he be taught to live openly with his diabetes. If guided correctly, he will become a healthy, hardy child and there is no pleasure of youth he should not enjoy as long as he knows how such will influence his diabetes and what to do about it. The girls will grow into normal womanhood and should not be denied marriage (preferably to a nondiabetic) or motherhood.

You may feel that I have put undue tedious emphasis on some phases of diabetic care in children, or have been a bit too elementary. Even with our present knowledge I continue to see many tragedies, either the fault of uninformed parents or equally uninformed doctors. For example, in our own teaching hospital a husky 11 year old girl was admitted recently with a picture of unconsciousness, dyspnea, fever, dehydration of, the parents claimed, only twenty-four hours duration from the onset. She was sent to the polio ward and a diagnosis of diabetic coma first suspected when a high spinal blood sugar was found. She died.

Another youngster was seen at home by her physician for abdominal pain and vomiting. She was given hypodermic sedation while the doctor rushed on to a "delivery." She was quieted—in fact, went on into diabetic coma from which she could not be revived. There are others.

It is to be hoped, and entirely possible, that within the life span of diabetic children another great advance in therapy may come about. Until then, we must utilize our present rather satisfactory knowledge to the best advantage.

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CURRENT TREATMENT OF HYPERTHYROIDISM*

A. SELDON MANN, M. D.†

NEW ORLEANS

Hyperthyroidism occurs in (1) diffuse goiter of Grave's disease (known as primary hyperthyroidism), (2) toxic nodular or adenomatous goiter or (3) single adenoma. For successful management of these diseases any of a number of therapeutic measures may be employed. These include medications, such as iodine (I^{127}) (Lugol's solution), thyroid extract or thyroxin sodium, antithyroid drugs (propylthiouracil and others) and radioactive iodine (I^{131}); surgical measures; and rarely radiation. Treatment may appear complicated because of the multiple choice of methods available for successful amelioration of symptoms. On the contrary, because of a better understanding of thyroid gland physiology and the availability of antithyroid drugs, radioactive iodine, and refinements in surgical techniques, the phy-

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sician may now plan treatment to meet the needs and combat the problems of each individual case. Planning of effective therapy depends upon consideration of the type of goiter producing the hyperthyroidism, determination of the extent of the associated complications, and finally, evaluation of the emotional and economical aspects of each individual case.

DIFFUSE GOITER WITH HYPERTHYROIDISM

The usual patient with uncomplicated hyperthyroidism associated with a diffuse goiter of Grave's disease presents no major problem in choice of treatment. Most of these patients are less than 45 years of age and for this reason alone the use of therapeutic doses of radioactive iodine is more or less universally discouraged because the long range side effects of this type of radiation have not yet been determined. If it can be proved that these effects are not deleterious to other tissues and structures, this form of treatment will be ideal for all patients with primary hyperthyroidism. It is probably the treatment of choice in patients over 45 years of age because it is simple to administer, safe, economical, effective in reducing the size of the goiter, and followed by minimal recurrences and a high rate of permanent remissions. The only disadvantages are that it is not yet generally available and hypothyroidism results in 10 to 20 per cent of patients treated.

Another type of therapy which is effective against diffuse goiter is antithyroid medication. Propylthiouracil, which is most generally used, is well tolerated by most patients. Administration of 200 to 400 mg. daily in divided doses at six or eight hour intervals causes the toxic symptoms to begin to subside in five to ten days. The euthyroid state is usually reached in one to three months, depending on the degree of toxicity and the size of the gland. After the symptoms have been controlled and the basal metabolic rate has returned to normal, the same dosage schedule is continued for approximately nine months. During treatment the patient should be examined at six to twelve week intervals for evidence of toxic symptoms or hypothyroidism. Development of toxic symptoms is an indication for substitution of another antithyroid drug or another type of therapy. Hypothyroidism can be controlled by adding 1 to 2 gr. of dessicated thyroid extract daily. This form of treatment is probably most effective in patients with small to medium sized glands. It is economical, produces no loss of time or permanent complications and the thyroid is intact during remission. Its greatest disadvantage is the rather high recurrence rate, which varies from 25 to 50 per cent depending on the selection of cases. Other disadvantages are slow control of symptoms, continued or progressive enlargement of the gland and prolonged medication and observation.

A third method of treatment consists in subtotal thyroidectomy after a euthyroid state has been produced by antithyroid medication. In the preoperative management 200 to 400 mg. of propylthiouracil daily in equally divided doses at six to eight hour intervals is given until all symptoms have disappeared and a euthyroid state is obtained. Lugol's solution is given, 10 drops daily for two or three weeks prior to operation, to effect involution of the gland. Properly prepared patients, improved surgical technique, and the antibiotics make operation relatively safe and the treatment of choice for patients with a large diffuse goiter or one which is suspected of being malignant. The advantages of surgical excision are early control of hyperthyroidism and removal of the undesirable mass. The operative mortality rate is less than 1 per cent. This method of treatment is less economical, is followed by complications such as tetany or vocal cord paralysis in from 0.5 to 5 per cent of cases and hypothyroidism in 10 to 20 per cent of cases, and the recurrence rate approaches 15 per cent. From these brief considerations the treatment of choice can readily be determined roughly, at least initially, by the age and economical status of the patient and the size of the gland.

TOXIC NODULAR GOITER

Treatment of nodular goiter with hyperthyroidism without serious complications

is surgical. The operative procedure is usually highly successful, the postoperative complications are minimal, the unsightly mass is removed and recurrences are rare. Though the occurrence of carcinoma in these goiters varies from 1 to 19 per cent in reported series, its development is a definite possibility which can be abolished only by surgical excision. These patients should be prepared for operation by administration of adequate doses of antithyroid drugs (propylthiouracil). The amount of drug and time required to bring about a euthyroid state may be greater than for primary hyperthyroidism. The terminal use of Lugol's solution preoperatively is not necessary.

If for any reason operation is contraindicated, adequate therapeutic doses of radioactive iodine are effective provided the tracer dose uptake study indicates a definite avidity for iodine. If both operative treatment and use of radioactive iodine are contraindicated, antithyroid drugs alone will control the symptoms. The major disadvantages of radioactive iodine and antithyroid drugs are slowness in attaining a euthyroid state, prolonged period of observation, persistence of the goiter and uncertainty as to the presence of carcinoma.

SINGLE ADENOMA WITH HYPERTHYROIDISM

There are conflicting opinions as to whether single nodules occur in hyperthyroidism. In large series of reported cases in which a single nodule was suspected clinically, multiple adenomas were present in the surgical specimen more often than not. In any event, when a single toxic nodule is suspected clinically, the treatment of choice is surgical. The relatively high incidence of carcinoma found in single adenomas may depend on whether the pathologist is "an optimist or pessimist;" nevertheless the therapeutic approach is surgical. The disadvantages of the use of radioactive iodine and antithyroid drugs are the same as in toxic nodular goiter.

COMPLICATED CASES OF HYPERTHYROIDISM

Because of the trend toward conservative use of radioactive iodine, at least in some areas, in patients with hyperthyroidism less than 45 years of age, it seems pertinent to mention some of the situations in which the choice of treatment is restricted to radioactive iodine in spite of age and other factors. These include recurrent hyperthyroidism in diffuse toxic goiter following one or more thyroidectomies, primary hyperthyroidism after the age of 45 years, hyperthyroidism complicated by serious cardiac or concurrent disease in which operation is inadvisable, recurring or persistent hyperthyroidism after use of antithyroid drugs, and occasionally, preference of the physician or patient for various reasons. Under these circumstances, an attempt is made to give an initial dose of I^{131} that will relieve the symptoms but not cause hypothyroidism. The optimum dose depends upon the estimated weight of the gland, the percentage of I^{131} uptake in twenty-four hours after a test dose of 100 microcuries indicating the avidity of the gland for iodine. Accumulated experience indicates that the average therapeutic dose in primary hyperthyroidism ranges from 5 to 10 mc. In toxic nodular goiter usually 8 to 20 mc. doses are required. Experience has also shown that in some as little as 3 mc. may produce hypothyroidism whereas in others as much as 100 mc. may be required to control the symptoms. Previous administration of iodine will influence the percentage of uptake in the test dose as well as the avidity of the gland to radioactive iodine in the therapeutic dose. Iodine can be used advantageously in severely toxic patients immediately following the therapeutic dose of I^{131}, since it is possible to precipitate a "thyroid storm" in some cases. If antithyroid drugs have been administered previously, their use should be discontinued for several days before radioactive iodine is given. A euthyroid state can be restored in those patients with hypothyroidism by adequate replacement therapy of dessicated thyroid extract or thyroxin sodium.

CONCLUSION

Successful treatment of hyperthyroidism

depends on application of the most suitable of the multiple choice methods available for treatment: medications, surgical therapy and rarely radiation. Selection of treatment should be based on knowledge of the type of goiter producing it and evaluation of the emotional and economic status of the individual.

DISCUSSION

Dr. Haydn H. Cutler, (Monroe): This summary of the current treatment of hyperthyroidism by Dr. Mann has been most complete and aptly presented. I would like to emphasize the emotional aspect of this disease, especially in relationship to its etiology and therapy. In order to understand the underlying factors in the production of this disease, one must remember that the thyroid gland is under the control of the pituitary gland which produces a thyroid stimulating hormone; in addition, the thyroid has a close inter-relationship with the other endocrine glands. Normally, it consists of acini which are lined by a low cuboidal epithelium and the lumina are filled with colloid. The production of more thyroid hormone is stimulated by the thyroid stimulating hormone, which causes an increase in the growth of the epithelium, which now becomes tall columnar, and also decreases the colloid content within the gland. The administration of iodine increases the colloid within the acini and also, there is a decrease in the size of the epithelial cells. Thiouracil, however, prevents the formation of thyroxin by the gland resulting in an exaggeration of the underlying pathological findings of increased hyperplasia of the lining epithelium.

The causes for the increase in the pituitary hormones is not known, but if one is an advocate of Selye's general adaption syndrome, then we could well assume that hyperthyroidism is the result of stress which produces an adrenopituitary imbalance, with the resultant excess of thyroid stimulating hormone. Thus we can see, that stress produced by physical factors; trauma, infection, chemical agent, foreign protein, or pure emotional factors, may very well serve as a stimulus to the production of the thyroid stimulating hormone and the resultant secondary hyperthyroidism.

In conclusion, because of these stress factors, I believe that the therapy in the future should be more preventive and directed toward alleviating mental and physical factors producing the stress and this future attack could be much more effective than all the anticipated advances in newer drugs and isotopes.

HYPERSPLENISM*

DANIEL W. HAYES, M. D.†
NEW ORLEANS

The normal spleen is an organ in which control of blood cell formation, blood cell sequestration, and blood cell destruction are balanced physiologic functions. Consequently, any imbalance in this physiologic equilibrium may give rise to clinically recognizable syndromes. Hyperfunction of any or all of these phenomena is called hypersplenism.

PHYSIOLOGY

Removal of the spleen causes certain almost indisputable changes in the blood elements. The red count usually rises slightly. Often target cells and cells with Howell-Jolly bodies appear. The white blood count often doubles itself with a higher rise in lymphocytes than in the neutrophils. The platelets are increased to high levels. These blood changes, after removal of a normal spleen, suggest that the spleen is at least a governor or controlling agent for the bone marrow.[2, 10, 11] It probably also acts to phagocytize old blood elements, especially red blood cells. These have been two sharply differentiated theories in the past though most will agree that there is truth in both views in the light of present knowledge. Doan[5] and Wiseman have been the foremost proponents of the excess phagocytic theory to explain these "hypersplenic syndromes," whereas Dameshek and co-workers[8] believe that hormones controlling the bone marrow, or lysolecithin[7, 8] may be produced by the spleen. Recently it has been considered that immune bodies play a prominent role.[4] Hypersplenism, then is hyperactivity of the spleen through one or more of the several mechanisms affecting the red cells, white cells, platelets or all three formed elements.

The hypersplenic effect on the white cells results in leukopenia. This is often found in splenomegaly from any cause. Neutro-

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penia occurs in variable degree from mild neutropenia to virtual agranulocytopenia.

The thrombocytopenia resulting from the hypersplenic syndrome is clinically evident as idiopathic thrombocytopenic purpura. However, thrombocytopenia is not always idiopathic, and other causes may be evident.

Hemolytic or nonhemolytic anemia may be present alone or combined with the other cytopenias. Secondary, as well as primary causes play a role in the production of these entities.

SPLENOMEGALY

The anatomic enlargement of the spleen may or may not be associated with hypersplenism. Splenomegaly alone is not the sole criterion of hypersplenism. The pathologic physiology of hyperfunction of the spleen must be present before hypersplenism may be diagnosed.

The list of causes of splenomegaly touches on all classes of disease. The infectious splenomegaly includes acute as well as chronic infections with some related collagen diseases. Congestive splenomegaly occurs in Banti's syndrome, cirrhosis of the liver, or portal or splenic vein thrombosis. The neoplastic and excessive cellular proliferation in the spleen is seen in leukemias, lymphomas, polycythemia vera, and myeloid metaplasia of the spleen. Certain cysts and tumors may cause splenomegaly. When there seems to be excessive blood destruction as in chronic or acute hemolytic anemias, hemoglobinurias or other chronic anemia, the spleen may be enlarged. Disorders of lipid metabolism and other infiltrative diseases may be grouped together.

HEMOLYTIC ANEMIA

Hemolytic anemia is most frequently unassociated with hypersplenism. In certain cases, however, functional hyperactivity of the spleen is closely linked to this disease. Familial hemolytic icterus, and a few cases of acquired hemolytic anemia are thought to be due to hypersplenism. Hypersplenism and splenomegaly secondary to leukemia, lymphoma, and certain infections will also cause hemolytic anemia.

In familial hemolytic icterus (congenital hemolytic jaundice or hereditary spherocytosis) the trait is a Mendelian dominant transmitted by either parent. In this condition spherocytes with increased fragility, a slight anemia, and an increased number of reticulocytes will be present. During crises spherocytosis is more marked; reticulocytes, leukocytes, and thrombocytes are reduced in the peripheral blood. A maturation arrest is present in the bone marrow during crisis. Increased indirect bilirubin is in the blood. The spleen is enlarged and maye be huge. Gall stones often occur as a complication of this disease. Splenectomy is in most cases curative. The pathogenesis of the disease is thought to be due in part to the destruction of the fragile spherocytes by the spleen or perhaps to the production by the spleen of abnormal hemolysins which coat the red cells, thus rendering them more fragile.

Acquired hemolytic icterus due to various causes may or may not be due to splenic overactivity. If there is a known cause, the underlying etiology should be treated. However, if the anemia is due to unknown cause, and particularly, if the direct and indirect Coombs test are both positive, there may be evidence of abnormal agglutinins and hemolysins in the serum.[8] In these cases splenectomy is most often of some value.

NEUTROPENIA

Neutropenia is seen in most cases of splenomegaly regardless of cause. Symptoms usually are of weakness and a tendency to repeated infections. It is important in these cases to have bone marrow studies in order to correctly ascertain that the bone marrow does not show a reduced number of granulocytes. In most cases of splenic neutropenia the myeloid series is perfectly normal, or there is a maturation arrest at the myelocyte or metamyelocyte stage without older forms present. The erythroid elements and the platelets should be normal in the bone marrow. Usually more extensive studies should be undertaken with particular care in order to rule out leukemia, lymphoma or infectious diseases which would respond to appropriate medical therapy.

The spleen is thought to function in these

cases to block the delivery of the granulocytes, to induce a maturation arrest or to abnormally phagocytize the cells. In appropriate cases, then, splenectomy will often be of value. Since the pathologic examination of the spleen may reveal a hitherto undiscovered disease in that patient, some care must be used to avoid an overoptimistic prognosis.[9, 11]

THROMBOCYTOPENIA

Thrombocytopenia due to hypersplenism is present as idiopathic thrombocytopenic purpura. It is well known and seems to occur in young females predominately. No definite inherited trait has been clearly identified, though there is often a family history of easy bruising. Purpura is the presenting symptom and the bleeding may occur in any body surface, organ, or cavity. The spleen is usually not demonstrably enlarged in more than 30 per cent of cases. The blood findings are characteristically those of thrombocytopenia with abnormal platelet forms seen in the peripheral blood. Bleeding time is usually prolonged and the clot fails to retract. Megakaryocytes are increased in the bone marrow and there is usually morphologic change of these elements. The pathology of the spleen may not show destruction of platelets.[11]

Since initial episodes, especially in the young, are often spontaneously improved and cured, splenectomy does not need to be done in each case. ACTH and cortisone have been of considerable help in reducing the acute purpuric manifestations; therefore, splenectomy may not have to be performed in the acute phase of the disease when there is a higher mortality. Certainly, it is to be performed in patients with repeated purpuric episodes or if bleeding persists despite treatment. In females who menstruate regularly splenectomy may be considered more strongly than in males. Recurrence is said to be higher in women than in men and splenectomy can be considered also from that viewpoint. Splenectomy is contraindicated if the diagnosis is not clear. If the splenectomy can be performed after the initial acute attack subsides the mortality statistics favor splenectomy as the treatment of choice. It remains to be seen whether ACTH and cortisone will change that statement materially.

Platelet agglutinins in the serum have been recently found in many cases which may be a significant and important factor in the destructive mechanism and decreased platelet count. These have been found in the more chronic cases rather than in the acute syndrome.[4]

PANCYTOPENIA

Splenic pancytopenia may occur with or without hemolytic anemia. If there is no hemolytic process there is evidently no excess destruction of the red cells by the spleen but if increased hemolysis occurs there is excess phagocytosis of the red blood cells in the spleen,[2, 3] in addition to an inhibitory effect on the production and/or the delivery of the cells to blood. Dameshek and coworkers[2, 3] do not believe that there is phagocytosis of other than the red cells to any extent and then only in hemolytic processes.

DIAGNOSIS

Diagnostic procedures in these cases must include complete peripheral blood studies, bone marrow examination, and perhaps other diagnostic procedures. The adrenalin test has been used extensively by Doan[5] but the validity of the procedure to demonstrate excess phagocytosis by the spleen has been in some doubt. Splenic puncture[1, 6] may be valuable in certain cases, mainly to rule out important secondary causes that would contraindicate splenectomy. The procedure is not without risk and some mortality. It has been used in Europe more than in this country for many years and it is said by Moeschlin[6, 12] to be attended with little danger.

Splenectomy and the response of the patient and his disease thereto is, in the final analysis, the true diagnostic test in the evaluation of hypersplenism. It must be emphasized again that hypersplenism is a functional, not an anatomic diagnosis and that the pathologic physiology which occurs as a result of hypersplenism may affect one or all of the formed elements of the blood. About 80 per cent of all cases of hypersplenism will be cured by splenectomy.[2]

Pathologic studies[11] seem to support the

theory that there is something else besides phagocytosis alone causing the various cytopenias. It is difficult to conceive of an accessory spleen the size of enlarged lymph node having the ability to phagocytize enough cells to cause a fully developed clinical syndrome of hypersplenism.

SUMMARY

Hypersplenism is a functional diagnosis related to the pathology physiology of an overactive spleen. Splenomegaly usually accompanies this deranged activity of the spleen but splenomegaly is by no means the one and only criterion to the diagnosis of hypersplenism. Primary disease of the spleen or secondary or systemic causes may cause hypersplenism.

Neutropenia, hemolytic anemia, thrombocytopenia, or pancytopenia with or without hemolytic anemia are the characteristic results of overactivity of splenic function.

The effect of certain unidentified splenic "hormones"[10] to inhibit bone marrow production or to prevent delivery of the cells to the peripheral blood has been postulated as the most likely cause of the clinical syndrome. Phagocytosis of red cells also plays a less prominent part in hemolytic syndromes. Autoimmune bodies and agglutinins are present in many cases.

Splenectomy is the treatment of choice in hypersplenic syndromes in which the diagnosis has been carefully evaluated. If all other causes which could be treated medically have been excluded, the operation will produce good results in four out of five patients.

REFERENCES

1. Block, Matthew, Jacobson, L. O.: Splenic puncture, J. A. M. A. 142:641 (Mar.) 1950.

2. Dameshek, William, Estren, Solomon: Hypersplenism, M. Clin. North America 34:1271 (Sept.) 1950.

3. Dameshek, William, Estren, Solomon: The Spleen and Hypersplenism, New York, Grune and Stratton, 1947, 55 pp.

4. Dameshek, William, Stefanini, Mario: Idiopathic thrombocytopenic purpura. Some ideas on its pathogenesis and treatment, M. Clin. North America 37:1395 (Sept.) 1953.

5. Doan, C. A.: Hypersplenism, Bull. New York Acad. Med. 25:625, 1949.

6. Moeschlin, S.: Quoted by Block, Matthew, Jacobson, L. O.) p. 641.

7. Scheff, G. J. Awny, A. J.: Lecithinase activity in splenic dyscrasias, Am. J. Clin. Path. 19:615 (July) 1949.

8. Singer, Karl, Miller, E. B., Dameshek, William: Hematologic changes following splenectomy in man with particular reference to target cells, hemolytic index and lysolecithin, Am. J. Med. Sci. 202:171 (Aug.) 1941.

9. Symmers, Douglas: Splenomegaly, Arch. Path. 54:385 (March) 1948.

10. Ungar, Georges: Endocrine functions of the spleen and its participation in the pituitary—adrenal response to stress, Endocrinology, 37:329 (Nov.) 1945.

11. Von Haam, E., Awny, A. J.: The pathology of hypersplenism. Am. J. Clin. Path. 18:313 (April) 1948.

12. Wintrobe M. M.: Clinical Hematology, Philadelphia, Lea and Febiger, 1952, 1048 pp.

DISCUSSION

Dr. A. J. Hertzog (New Orleans): Dr. Hayes has covered the subject of hypersplenism very completely and leaves me little to add.

Some years ago at the University of Minnesota, I looked up all of the cases of essential thrombocytopenic purpura that came to autopsy in a series of 20,000 consecutive autopsies. In 20 adults the average of weight of the spleen was 232 grams. The spleen then in essential thrombocytopenic purpura is only slightly enlarged and is rarely palpable. When we can palpate the spleen the purpura is usually not the idiopathic variety. Microscopic sections of the spleens in essential purpura show practically a normal histologic picture. Some investigators like Von Haam have described minor alterations of the reticulum of the spleen in essential purpura but such findings are not generally accepted. In the bone marrow in essential purpura we usually find marked hyperplasia of the megakaryocytes. There is decreased platelet production and immaturity of the nuclei of the megakaryocytes. Hence, I think the best interpretation of essential thrombocytopenic purpura is that it represents a variety of hypersplenism with a failure of the megakaryocytes of the bone marrow to produce platelets. Where the megakaryocytes are numerous in the bone marrow excellent results are usually had following a splenectomy. Poor results are usually expected where the megakaryocytes are reduced in number.

An enlarged spleen is found frequently in Hodgkin's disease. We may get signs of hypersplenism such as anemias or leukopenias or thrombocytopenias with any enlarged spleen, regardless of the cause of the splenomegaly. In recent years it has become recognized that some of these cases of malignant lymphoma can get temporary benefit with marked improvement of their anemia, thrombocytopenia, or leukopenia following a splenectomy. However, in these cases it is necessary to show that hypersplenism exists by bone marrow studies before one is justified in doing a splenectomy. It should also be recognized that the procedure is more or less palliative therapy.

The spleens removed at operation from congenital hemolytic icterus are always enlarged, dark red, and show marked congestion of the pulp with red blood cells. The fundamental pathology in congenital hemolytic icterus is not in the spleen but in the red blood cells. Fat round spherocytes are found in this disease. These cells are abnormally fragile. One of the normal functions of the spleen is to destroy red blood cells and hence these

abnormal cells are excessively destroyed. Splenectomy is curative as a rule in these cases as it removes the principal source of red cell destruction for these fragile spherocytes. Hence, congenital hemolytic icterus represents a variety of hypersplenism where the normal phagocytic property of the spleen is at fault rather than any hormonal mechanism that it may exert on the maturation of cells in the bone marrow.

I think we have a tendency to oversimplify the complex mechanisms discussed under the term of hypersplenism. However, such conceptions as brought out by Dr. Hayes do give a clinician a practical approach to splenic malfunction and in properly selected cases splenectomies are of great benefit to the patient while in other cases the patient is not benefited and may actually be done a great deal of harm by an ill advised splenectomy, particularly in the syndrome commonly known as agnogenic myeloid metaplasia of the spleen.

The spleen is one of the most difficult organs for a pathologist to interpret either histologically or cytologically. Hence, I think splenic punctures with a needle are of very little diagnostic value because of the difficulty of properly interpreting the small piece of tissue or cells obtained. The limited value is offset by the danger of severe hemorrhage from a congested spleen following a needle puncture. Hence I do not recommend splenic punctures as a diagnostic procedure, with the exception of a very exceptional case where someone is trying to establish a diagnosis of a rare parasitic disease in the presence of a splenomegaly.

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DIAGNOSIS AND TREATMENT OF HYPOPITUITARISM*

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DIAGNOSIS

Hypopituitarism is an unusual disease, which is not too difficult to diagnose if it is suspected. One can hardly blame any physician for not making the diagnosis, since the usual textbook description of the disease is misleading. Indeed, cachexia was thought to be so essential in the diagnosis that the disease is most commonly referred to as Simmond's cachexia. Unfortunately, it is one of the least common symptoms. Indeed, in patients with cachexia, anorexia nervosa, malignancy or advanced tuberculosis should always be considered as more likely diagnoses than panhypopituitarism. The disease most commonly encountered manifesting cachexia and mimicking panhypopituitarism is, of course, anorexia nervosa. Whereas from many laboratory aspects, anorexia nervosa might well be considered as hypopituitarism, it is a psychogenic disturbance. However, the laboratory and clinical findings relative to hypopituitarism in this disease are real. There has actually been a decrease in pituitary secretion. This is part of the body's attempt to defend itself against severely inadequate nutrition and can be induced experimentally in animals by underfeeding. This state of "pseudo-hypophysectomy" also occurs in various degrees in certain other chronic diseases, such as extensive cancer.

Anorexia nervosa usually occurs in young unmarried women. They are severely emaciated individuals with amenorrhea and many of the laboratory findings of panhypopituitarism. Surprisingly enough the mammary tissue remains unchanged despite loss of body substance and amenorrhea. In such cases the prognosis can be poor, although it has sometimes been possible by administration of ACTH and cortisone to increase the appetite, and, with adequate psychogenic support, to effect wht amounts to a cure. There are also remissions in many cases due solely to adequate psychotherapy. The other possible approaches, such as forced feeding and the like, are beyond the scope of this paper.

The patient with panhypopituitarism, on the other hand, presents a long story of fatigue, mental slowness, loss of pubic and axillary hair, and even social withdrawal to the extent of being classified as psychotic; they are in general quite unhappy individuals. Females also complain of amenorrhea, and males, impotence. They are often able to carry on only at a low level of activity and can barely care for themselves. They also have anemia, which is usually refractory to standard anti-anemic measures.

It has been our experience that the com-

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monest form of the disease follows a difficult delivery accompanied by severe hemorrhage. This type, first fully described by Sheehan, bears his name. In these patients following delivery the clinical picture is one of additional shock, failure to lactate, postpartal amenorrhea, and loss of pubic and axillary hair. Such patients often comment that the pubic hair failed to regrow after the shaving for delivery.

In many of these patients the clinical picture and laboratory findings are almost indistinguishable from those of primary athyreogenic myxedema. Although it is theoretically possible to distinguish them on the basis of thyroid stimulating hormone titer in body fluids, there is at present no readily applicable clinical method for determining this. There is a suggestion that they may be distinguished by the use of thyroid stimulating hormone (T.S.H.) and repeat I^{131} uptakes. The major reason for concern about these patients is that if the myxedematous appearance is due to panhypopituitarism the administration of thyroid may constitute sufficient stress to the patient to precipitate adrenal crisis, and even on occasion, subsequent death.

Panhypopituitarism can also be present with symptoms referable only to low adrenal function. All the clinical manifestations of classical Addison's disease are present except one. There is no increase in pigmentation when the Addisonian picture is of hypophyseal origin.

In order to diagnose panhypopituitarism it is necessary to think of the specific disease itself. In patients with fatigue, anemia, and amenorrhea, or impotence, a search for loss of axillary hair should be routinely made. This will greatly increase the incidence of recognition of these cases. It must be remembered, however, that some normal patients have congenitally absent axillary hair and some men never have facial hair.

Once the disease is suspected, it is considerably easier to diagnose. The means of establishing the diagnosis of panhypopituitarism are available to almost everyone. In at least one third of the patients destructive lesions in the area of the sella turcica can be demonstrated roentgenographically. The basal metabolic rate is low, often without the concomitant increase in cholesterol which is usual in athyreotic myxedema. The fasting blood sugar is usually low and there is a flat glucose tolerance curve. The water-load test for adrenal reserve (Kepler test) usually yields a positive result. The eosinophile count is often high and a four hour ACTH test ordinarily produces no significant decrease in the eosinophiles. Use of the epinephrine test with the eosinophile counts and uric acid/creatinine ratio has been of no assistance to us in a differential diagnosis of the illness. We do believe that the standard forty-eight hour ACTH tests are of help, since the patients usually do not respond early, but by the end of the test there is a definite response showing eosinopenia and usually ketosteroid and corticoid response in the urine. In the larger medical centers where it is possible to obtain specific endocrine bioassays, the 17-ketosteroid excretion, corticoid excretion, gonadotropic hormone excretion (measured by any one of several methods) and prolactin excretion all have low values, which would serve to confirm this diagnosis.

TREATMENT

Once the diagnosis is established, one is faced with the problem of therapy. This, of course, being specific hypopituitarism, is ideally treated by substitution therapy with pituitary hormones. Unfortunately, the only one of these which is available in clinically active form for prolonged therapy is the adrenocorticotropic hormone (corticotropin or ACTH). Surprisingly small doses of ACTH suffice to induce dramatic improvement in the status of these patients. The usual maintenance dosage is 10 units of highly purified ACTH gel daily or every other day.

In some patients it is also necessary to treat accompanying hypothyroidism. Unfortunately, the available preparations of thyroid stimulating hormone have a great propensity for the production of antihormones and, therefore, it is usual to employ

substitution therapy with thyroid. Usually the maximum tolerated daily dosage is from 1 to 2 grains USP thyroid. The same unfortunate status of affairs with regard to replacement of gonadal function by administration of pituitary gonadotropic hormone preparation exists, as with T.S.H. Therefore, in those instances in which gonadal function should be restored it is best done by administration of either estrogen or androgen.

There is no adequate, commercially available preparation of growth hormone for use in humans and, as far as I know, no successful use of any growth hormone preparation in panhypopituitarism. However, it is entirely possible to employ androgens, either methyl testosterone or testosterone propionate, for their anabolic effect in this state. Indeed, it is often possible to treat women satisfactorily with testosterone propionate alone for panhypopituitarism. This does not restore gonadal function but otherwise often provides complete replacement therapy.

A comparison of the cost of the various types of therapy is especially important, since these patients require life-long replacement therapy. The most recent costs available for our most typical therapeutic program are listed in Table I.

TABLE I

1.	Testosterone propionate in oil 25 mg/day	$.49
2.	Thyroid U.S.P. grs. 2 daily	$.02
	Cortisone acetate 25 mg/day	$.23
	Desoxycorticosterone acetate 2 mg (Buccal)/day	$.15
	Methyl testosterone 20 mg/day	$.30
		$.70
3.	H.P. ACTH gel 10 units/day	$.60

SUMMARY

The diagnosis and treatment of panhypopituitarism has been discussed. We would particularly urge its consideration in patients with decreased or absent axillary hair.

DISCUSSION

Dr. Paul J. Murison (New Orleans): In this presentation Dr. Segaloff wisely stressed what the relative rarity of hypopituitarism has obscured, namely, that if one keeps the possibility in mind the diagnosis of hypopituitarism is not difficult to make. One suspects that many patients with this condition go unrecognized—labeled psychoneurotics or anemias of unknown etiology. Certainly, the majority of patients whom we have seen give stories of having seen many physicians over periods of one to ten or more years without the true etiology of their complaints being suspected. In all these cases, an inquiry about menstrual history in women, or about sexual habits in men and an inspection of pubic and axillary hair, should have at least suggested the possibility of hypopituitarism. The uncommonness of this condition should not lull us to indifference because with present therapy, to correctly recognize the condition is to rehabilitate an incapacitated person.

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SURGICAL ASPECTS OF PANCREATITIS

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Among major surgical problems, there is no more debatable subject than that concerning the value of surgery in pancreatitis. Many, perhaps most, of the ablest and most prominent members of the surgical profession feel that for severe acute attacks conservative measures only are indicated and that for chronic or recurrent attacks of pancreatitis an indirect approach for the control of pain or pancreatic secretions is the proper treatment. On the other hand an increasing group of surgeons take a more aggressive attitude toward the treatment of pancreatitis and it is this type of policy and its results which I wish to present.

In this paper primary pancreatitis only is considered and not pancreatitis secondary to other inflammation such as penetrating ulcer. A few definitions seem necessary to establish points about which controversy admittedly might ensue. What is meant by pancreatitis clinically, and what is objective evidence of pancreatitis at the operating table? From a clinical standpoint, a certain group of symptoms and objective findings must be present to justify placing a case in the category of pancreatitis. No strict definition of this will have to be considered here because all of the cases pre-

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sented herein are those confirmed at the operating table. On the other hand, it is very important in comparing results of a group of patients treated conservatively and those treated surgically, to have some agreeable definition of what might be considered pancreatitis prior to the operation. It is not possible to deny that any patient who has pain in the upper abdomen radiating through to the back, of a recurrent and severe type with tenderness and rigidity, particularly in the upper mid-abdomen during the attack, possibly associated with more pronounced symptoms relative to the gall bladder area and certainly, those with elevated amylase values during the acute attack or elevated lipase values during its abatement, and those with a widened duodenal loop on roentgenographic examination may be considered probabale, if not actually proven cases of clinical pancreatitis.

Objective evidence at operation justifying the diagnosis of pancreatitis may be present in relatively severe form where the diagnosis has been other than this, such as cholelithiasis, ruptured ulcer, and intestinal obstruction. At the operation the following signs are evidences of pancreatitis:

1. Firmness, or hardness of the pancreas: This increased consistency involves usually not only the head but the entire gland. It is important for the surgeon to run his hand along the entire organ to determine whether the body and the tail are uniformly involved in these changes. The maximum change frequently is in the head and it may be less noticeable in the body and tail, but when pancreatitis is present, it practically always involves to a greater or lesser extent the entire organ.

2. Enlargement of the pancreas is a constant finding in pancreatitis. It may vary from slight to many times the normal size.

3. Spotted fat necrosis is a sign of pancreatitis. This is found particularly in the region of the pancreas, but it may also be encountered in various areas throughout the abdomen.

4. Brownish fluid exudate in the upper abdomen, and particularly, in the lesser peritoneal cavity with other signs is indicative of hemorrhagic pancreatitis.

5. Necrosis of the pancreas—the finding of grumous soft material is a most valuable sign in establishing the diagnosis.

6. In addition to this, the root of the mesentery should always be carefully palpated as it comes out from under the transverse mesocolon. If it is thickened and edematous and there is marked edema along the gastrohepatic ligament, these are additional signs of acute pancreatitis.

7. Biopsy of the pancreas with a positive diagnosis of pancreatitis or necrosis further establishes the diagnosis, but even this must not be taken as absolute evidence to the exclusion of other possibilities because pancreatitis may co-exist with other lesions, notably a neoplasm. Pancreatitis associated with neoplasm of the pancreas in our series has been excluded from this report and discussion.

Without attempting to elaborate on the pathology in this surgical consideration, a brief classification is acknowledged for those who are considering the justification for this aggressive viewpoint. The cases of pancreatitis are divided into:

1. Acute hemorrhagic pancreatitis, with or without sequestration of the pancreas.
2. Acute pancreatitis.
3. Chronic pancreatitis.
4. Recurrent pancreatitis.
5. Calcareous pancreatitis and pancreatic lithiasis.
6. Traumatic pancreatitis.

It is very difficult at the operating table, if one does not know the clinical history, to classify the disease pathologically on the operative findings. Of course, it is easy when there is an acute hemorrhagic pancreatitis with the evidence of hemorrhage and with a larger, tremendously swollen pancreas and fat necrosis. It is probably safe at the operating table to take fat necrosis as evidence of an acute attack, but what about a hard, enlarged pancreas, enlarged three or four times normal and iron hard, without fat necrosis or fluid in the abdomen. Can this not be acute pancreati-

tis? It certainly can, based on the clinical evidence, including high amylase reaction in some of these patients. The chronic variety is usually, from a clinical and operative standpoint, one in which there have been recurrent subacute or acute attacks, but which at the time of the operation, is not a remission. It is probably very rare for a low grade pancreatitis not to have exacerbations at least in the subacute phases. Regretfully, so far we have not taken pancreatic biopsies from every case. Although it is not very elegant or classical, I like to think of pancreatitis as being "low grade" or "high grade".

REVIEW OF CASES

During the last eight and one-half years, from January 1945, on our private services, we have encountered 10 cases of pancreatitis. These are all of the cases of pancreatitis, so far as I know, which I have treated during that period. During the same time it is notable that we have performed 204 cholecystectomies for diseased gall bladder.

The youngest of the 10 patients was twenty-three years old and the oldest sixty-five. There were 5 in the sixth decade of life, 2 in the fifth, 1 each in the third, fourth, and seventh.

Pain was the most constant subjective symptom and in the majority of patients it radiated through to the back. It was of a severe type, usually in the upper epigastrium and, in some instances, the more accepted variety of pancreatic pain, was overshadowed by the pain of gall stone colic. Two patients were jaundiced; one of these had stones in the common bile duct; the other had no gallstones. Six of the patients had or formerly had gallstones. Two had a perfectly normal gall bladder. One had cholecystitis without stones and one had cirrhosis of the liver, and normal gall bladder. Six of the patients had never been operated upon for anything resembling biliary or pancreatic disease. Two had had previous cholecystectomies, one had had cholelithotomy and cholecystostomy and one had had an exploration with gastroenterostomy.

The operative findings in three instances justified the diagnosis of severe, acute pancreatitis, on the basis that fat necrosis was found at operation with a tremendously enlarged, swollen pancreas, and edema involving the root of the mesentery and the gastrohepatic ligament. In one of these there was a brownish grumous material, and subsequent sequestration and drainage of necrotic tissue from the pancreatic bed. Biopsy was taken in only three of the entire group. In two the diagnosis of pancreatitis was confirmed and in one fat necrosis was reported.

Operation — Technical Features: Because of the attitude which we have that the disease is on an obstructive basis, the objective of the operations was always to decompress the biliary system. In 9 out of the 10 cases, a T-tube was placed into the common duct. In 7, the T-tube with multiple perforations, was permitted to traverse the ampulla of Vater into the duodenum. In one instance a cholecystotomy was done to decompress the biliary tract because the edema and swelling was so massive in and around the gastrohepatic omentum and the patient was so desperately ill, that choledochostomy was considered inadvisable. A transduodenal, as well as a supraduodenal exploration of the common duct was done in 5 cases. In 5 of the cases sphincterotomy was done. In the remaining, dilators were passed through the ampulla into the duodenum.

Results:—All of these cases recovered, and all of them have remained well subsequently, although 2 operated upon—1 in February 1953, and one in March 1953—still have a T-tube in the common duct. One of these has had an attack of pain in the abdomen on one occasion.

DISCUSSION

No consideration has been given to the etiology of acute pancreatitis. Since the classic report of Opie in 1901, the possibility of regurgitation of bile into the pancreatic system and activation of pancreatic autolysis always enters into a consideration of etiology. The lymphatic, neurogenic, virus, traumatic, and other theories deserve consideration but probably the weight of

evidence points to obstruction to pancreatic secretion and possible reflux of bile into the pancreatic ducts as the most common cause of pancreatitis.

In this presentation no mention has been made of other possibilities. Vagotomy, splanchnicectomy, and sympathectomy, pancreatectomy, pancreatic and/or common duct transposition, cholecystectomy, and more conservative measures should not be completely ignored. Certain of these procedures may be well indicated and of great value for selected cases, namely calcareous pancreatitis.

I am convinced that pancreatic disease deserves surgical consideration and that an aggressive attitude can give excellent results. During this time, we have probably overlooked cases of pancreatitis, not only clinically, but at the operating table, simply because we were not looking for them. In the last few years we have been more acute and more attentive to the diagnosis objectively and we are finding it with increasing frequency. When it is found at the table, we think there is justification for sphincterotomy, which was done in our last 4 cases and in 5 of the 10, the first one of the group having been done in 1948. This operation was first deliberately performed for this condition and was advocated by Archibald in 1929. Since then other authors have used and advised it with various technical modifications.

When the duodenum is opened, one may see that it is impossible to pass a 2 mm. dilator through the ampulla. I gain the impression that it is not the muscle which causes the obstruction, but that it is a mucosal ampullitis; that the small mucosal orifice tightens down and becomes constricted. It has the same appearance as that of the orifice of the submaxillary salivary duct when a stone is impacted therein. Under these circumstances no amount of pushing without actually bi-manually milking the small probe through the orifice will accomplish its passage. When these findings are present we then incise the ampulla, opening it widely, cutting the ampulla and the sphincter, assuring a free opening into the common duct.

In some instances, it is not feasible to find the ampulla of Vater even with the duodenum open. In one of the acute cases, we made a false passage with a dilator by forcibly pushing it into the swollen head of the pancreas. It was carefully readjusted and the mucosa in the region of the sphincter was cut in order to establish a good opening into the common duct, but in this case there was so much swelling of the pancreas that it was not feasible to put a long arm tube into the duodenum. I prefer this type of tube when a sphincterotomy has been done, to prevent stenotic healing of the ampulla, although admittedly this may not be absolutely necessary. When this is the choice, multiple perforations must be made in the vertical arm of the tube to prevent obstruction of the pancreatic duct by the tube and to insure the free escape of pancreatic secretions into the duodenum. In one case of acute hemorrhagic pancreatitis, decompression was accomplished by a cholecystectomy and in this patient also two small bowel catheter enterostomies were established. There is a tremendous swelling at the root of the mesentery in severe pancreatitis and this prevents decompression of the small bowel with a transnasal gastric tube. It produces in effect a Wilkie's syndrome, and the hard mesentery lying over the third portion of the duodenum prevents the retrograde escape of gas and fluid in attempted decompression by gastric suction. Because of massive swelling and the severe ileus in this case, two enterostomy tubes were placed—one at the lower end of the jejunum and one at the lower end of the ileum, to insure decompression. This patient had, in addition to the ileus and hemorrhagic pancreatitis, a chemical peritonitis and decompression by entepostomy in this instance may have been a life saving measure.

Two cases in this series are reported in detail to give some idea of the part surgery played in their management.

CASE REPORTS

One was a sixty-five year old man, the oldest individual in this group, who was on the first phase of a Mediterranean cruise. He became sick three days prior to the time I saw him, with severe

pain in the epigastrium, radiating through to his back. He had had five similar attacks in the last fifteen months. His physician in San Francisco, who referred him and with whom I talked on the telephone, told me that the patient had been studied at several prominent clinics there and elsewhere and that the diagnosis of recurrent pancreatitis had been repeatedly made, supported by high lipase levels as positive evidence. Objectively, he had tenderness in the upper abdomen with rigidity and a mass. The amylase values were normal, but I felt that he had acute cholecystitis and advised operation. I also felt that he probably had pancreatitis, but because he had seen many more eminent doctors, who had told him he had pancreatitis, but had never advised him to be operated upon for this, it seemed unwise for me to suggest that the operation was indicated even for the pancreatitis.

After brief hours of preparation, he was operated upon. The mass proved to be a very large head of the pancreas. The pancreas was about four times normal size. Fat necrosis was spotted in the upper abdomen. Tremendous edema was found involving the gastrohepatic omentum and the mesentery of the small bowel. The gall bladder was distended, edematous, acutely inflamed, but it did not contain stones.

At operation the common duct, which was dilated twice normal size, was opened. Thick, syrupy bile escaped. The obvious obstruction to the duct was so marked it made one wonder why clinical evidence of jaundice was not present. A small Bakes dilator could not be passed into the duodenum. The 2 mm. dilator was forced and it created a false passage between the duodenum and pancreas. Then the duodenum was mobilized, turned forward and an opening was made into it, and with a dilator through the supraduodenal opening in the duct as a guide, the duodenum was cut to secure an opening into the duct. A T-tube was placed in the common duct. This was a short arm tube which did not go into the duodenum. The gall bladder was removed. Drains were placed in Morrison's pouch and into the head of the pancreas, from which a small biopsy was removed with Allison forceps.

The opening in the duodenum was carefully closed and the T-tube in the common duct was permitted to come out through a stab wound in the right subcostal area. Because of the severity and nature of the illness necessitating proteolytic drainage, the patient was closed with through and through wire retention sutures as well as individual layer closure. He made an uneventful recovery. Subsequent cholangiograms, the last made in April 1953, have appeared perfectly normal.

This patient has remained well. He writes me that for the first time in two years he has felt perfectly normal and without fear of recurrent attacks, that he was going to the province of Quebec for three weeks for fly-fishing for salmon. He still has the T-tube in. I advised that it not be removed for a period of five or six months following his operation. He simply opens it and drains it for a period of about twenty minutes twice a day.

The second case to be reported to indicate the objectives of immediate surgical attack on pancreatitis was more complicated. The patient was age forty-two and when I saw him after he had been sick for five days he was under the care of able clinicians in a private hospital and they were then debating the diagnosis, feeling that there were some features suggesting intestinal obstruction.

The patient had been a relatively heavy drinker and he became ill in a small town in Louisiana, with severe upper abdominal pain radiating through to the back. Diarrhea, nausea and vomiting ensued with extreme weakness and prostration, board-like rigidity and tenderness of the abdomen, and massive distention.

When I saw him he was desperately ill with a protuberent belly distended as if it would pop. He was extremely toxic, delirious, and with signs of peritonitis.

The amylase test which was done three days after the onset of the illness was reported normal. Flat plates of the abdomen showed distended small bowel.

Operation was advised and within a period of hours after preparation it was undertaken. Through a right rectus incision the right iliac fossa area was first exposed, because intestinal obstruction seemed a likely possibility. A paraduodenal pocket was found into which the terminal ileum as it became overdistended apparently had gotten caught, and there was either an actual or a pseudo-obstruction at this point. This was released but it was not certain that this alone was the trouble. Furthermore fat necrosis was evident. In the upper abdomen was found a tremendous, swollen and edematous mesentery and gastrohepatic omentum with extensive fat necrosis and a brownish grumous material in the region of the duodenum. The gall bladder was distended but not acutely inflamed. The common duct was obscured by massive edema in the gastrohepatic omentum. The mesentery of the small bowel lay like a lead pipe across the third portion of the duodenum. The lesser peritoneal cavity was occupied by a tremendous mass.

Because the patient was so ill, it was felt that decompression of the biliary tract could be accomplished with less disturbance and with more facility, by putting a tube in the gall bladder, which was done. A drain was placed in the lesser peritoneal cavity onto the pancreas. An enterostomy tube was placed in the terminal portion of the jejunum and another one in the terminal portion of the ileum. The abdominal wound was closed. The patient had gradual improvement following this operation. The drains were removed on the thirteenth postoperative day and the enterostomy

tubes on the twelfth. He then subsequently developed a mass in the abdomen which we realized was a collection of pancreatic fluid and it was necessary to do a secondary drainage for this. At this second operation a necrotic pancreas was found. Larger drains were established in the pancreatic bed. He gradually improved and recovered. In the last few years he has refrained completely from alcohol and he has not had anything suggesting recurrence of the pancreatitis.

In reviewing the convalescence of this patient, the enterostomies proved of great value in decompressing the distended bowel. It was our impression that entertostomy sometimes may be of value in severe pancreatitis with severe ileus and tremendous distention, because mechanical decompression cannot readily be accomplished by gastric tube, owing to the obstruction of the duodenum by the swollen mesentery. This is the type of case in which today we would be inclined to use cortisone. It has been reported as favorably influencing the course of severe pancreatitis, but it would not be employed by us to the exclusion of surgery.

The favorable outcome in all of these cases depends in part on modern preoperative and postoperative measures. The use of antibiotics is extremely helpful and important and indeed this probably as much as any single improvement permits a more aggressive attitude toward the disease and makes active surgical attack now not only safe but possibly the safest method of management.

It is realized that this report does not prove that surgery is always indicated promptly for pancreatitis. It is offered only as minor evidence that this may be the correct attitude; that aggressive decompression of the biliary tract and ampullotomy are justifiable objectives to permanently cure primary pancreatitis of the acute or recurrent types.

REFERENCES

1. Archibald, E.: Acute edema of the pancreas; clinical and experimental study, Ann. Surg. 90:803, 1929.

2. Cattell, R. and Warren: Surgery of the Pancreas, W. B. Saunders Co., Philadelphia and London, 1953.

3. Doubilet, H. and Mulholland, J. H.: Recurrent acute pancreatitis; observations on etiology and surgical treatment, Ann. Surg. 128:609, 1948.

4. Mallett, Guy P., Jaubert de Beaujeu, M.: Bilan de la splanchnicectomie gauche dans le traitement des pancreatites chroniques recidivantes: D'apres 52 observations personnelles (1942-1951), Lyon. Chir. 47:531, 1952.

5. Mallett, Guy P., Bilan de la pancreatectomie gauche, Sud. Med. Chir. 85:1702, 1952.

6. Stephenson, Jr., Hugh E., Pfeffer, R. B., and Saypol, G. M.: Acute hemorrhagic pancreatitis. Report of a case with cortisone treatment, Arch. Surg. 65:307, 1952.

RECENT TRENDS IN MEDICAL TREATMENT OF ARTHRITIS*

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With the constant introduction of new drugs for the treatment of arthritis and rheumatism, management of patients with these diseases is dependent on a thorough understanding of the uses and limitations of these agents and the need for accurate diagnosis of the type of arthritis being treated. Arthritic patients encountered by the practicing physician can be classified into one of three groups. About one-third of the patients would fall into the group comprising rheumatoid problems, another third would be classified in the group of osteoarthritis, and the remaining third would be those whose disease was due to trauma, bacterial infection, palindromic rheumatism, gout, Reiter's disease, psychogenic rheumatism, psoriasis, and fibromyositis.

Treatment of arthritis is directed toward relief of discomfort, prevention of articular deformities, and correction of deformities that have already occurred. In addition, chemotherapeutic and antibiotic aids should be utilized to combat bacterial arthritis and psychotherapeutic assistance should be offered those with psychogenic arthritis. Appreciation of the insignificance of "foci of infection" as the cause of arthritis has virtually abolished the practice of routine tonsillectomy, dental extraction, prostatic massage, or administration of antibiotics as treatment for arthritis.

It has been our experience that adoption of a program of basic treatment routine offers the best means of accomplishing the foregoing aims of treatment. This implies

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proper rest, phychotherapy, arthritic exercises, orthopedic assistance (supports as well as operative) and general supportive measures (correction of anemia, diet, etc.). When combined with this basic program, the newer medical adjuncts, judiciously employed, will assure the patient with arthritis a complete program of therapy.

During the past few years a number of drugs have found a place in the medical treatment of arthritis. These include gold salts, cortisone and corticotropin (ACTH), hydrocortisone (Compound F), benemid, phenylbutazone (butazolidin) curare-like drugs and hyaluronidase. Time and experience have demonstrated their limitations and indications.

GOLD THERAPY

Gold salts have been used for the treatment of rheumatoid arthritis for twenty years but there are still differences of opinion as to their value. Despite the fact that some reliable investigators have been unable to demonstrate any benefit in their cases, gold salts are generally considered useful therapy for rheumatoid arthritis. Most observers would possibly agree that gold salts do help a majority of patients with rheumatoid arthritis in that a remission appears earlier than when just basic measures are employed. The same observers, however, would no doubt admit that the recurrence rate of rheumatoid arthritis certainly is unhappily high in the treated patients and it seems that at the end of five or six years those treated with gold fare little better than the others. For these reasons and also because of the possibility of development of reactions such as dermatitis, stomatitis, gastrointestinal toxicity, hematologic disorders and renal toxicity, many physicians are unwilling to treat the occasional patient with gold salts.

It must also be realized that the method of action of gold is not known. Moreover, gold should not be given before simpler basic measures have been tried or to patients in whom the diagnosis is in doubt, or fixation and deformities comprise the entire clinical picture. Advocates of gold therapy consider the patient with rheumatoid arthritis and active synovitis as the correct candidate for treatment.

Because it is believed that to be effective, gold must be absorbed in solution, the soluble salt (gold sodium thiomalate or gold thiogluone in oil) is recommended. Ten milligrams is injected intragluteally, followed one week later by an injection of 25 mg., and 50 mg. the third week; thereafter 50 mg. is injected at weekly intervals until from 16 to 20 injections have been given. The development of a reaction is an indication for discontinuance of the drug. If the patient shows no improvement after the twentieth injection, there is little reason to continue administration of the drug. Should improvement occur, however, maintenance doses of 50 mg. every two or three weeks indefinitely are believed by some to reduce the relapse rate, though this may be questioned.

Gold should be administered only by the physician versed in its limitations and dangers. Moreover, the patient should be informed of the need for continued medical visits, repeated blood counts and urinalyses, as well as the risks involved.

CORTISONE AND CORTICOTROPIN

The initial enthusiasm for the use of ACTH and cortisone as antirheumatic agents has now been replaced with a more practical working knowledge of when these drugs may be used for the greatest good. Not all patients with rheumatoid arthritis should be given these potent agents. First, it must be appreciated that neither drug can cause arrest of the development of rheumatoid changes despite the evidence of well-being which may result. Approximately 40 to 50 per cent of patients with rheumatoid arthritis are troubled with mild to moderately severe arthritis, manifested by fatigue and stiffness, slight swelling, and soreness of the involved joint. Most of them can get along by reducing the amount of physical activity, increasing the amount of rest, institution of physical therapeutic measures (with arthritic exercises) and use of sufficient amounts of aspirin. Because ACTH and cortisone have no effect on progress of the disease, nothing is gained

by using either drug in this group of patients. In the other 50 to 60 per cent of cases, many have already deformed joints with limited motion but no active systemic symptoms; again ACTH and cortisone would not help these patients. The remaining patients have acute debilitating involvement; in some of these at least temporary relief will be obtained by administration of ACTH or cortisone and in a small percentage this benefit will be more or less permanent.

Cortisone and ACTH may be considered for treatment of those patients with rheumatoid arthritis which is progressing rapidly despite employment of all other therapeutic measures. Those patients whose disease can be controlled with simple measures but who may be confronted with more trying periods which require their continued activity could also be given ACTH or cortisone for temporary assistance. It has been noticed that a few fortunate elderly persons with rheumatoid arthritis can be kept comfortable with small daily doses (25 mg.). Finally, in patients in whom an active program of corrective physical therapy is to be employed, these drugs may help facilitate motion by making the patient more comfortable.

ACTH is a definite aid in treating acute attacks of gout which may be resistant to colchicine or in a patient in whom a therapeutic dose may cause an unusual amount of gastrointestinal distress. In such cases 50 mg. of ACTH is given every six to eight hours until relief is obtained or a total of 200 mg. has been administered. It is necessary for the patient to take 1/100 gr. of colchicine three times a day or four times daily during administration of ACTH and to continue taking a daily dose so as to prevent recurrences following withdrawal of ACTH. If a patient cannot take colchicine three or four times daily, it should be given as often as tolerated.

When ACTH or cortisone is indicated for a patient with rheumatoid arthritis, the dosage should be kept as low as possible. It is no longer the purpose to alleviate all symptoms, but rather to diminish their intensity without producing hypercorticism. The choice of medication is usually dependent on the ease of administration. Cortisone probably should not be administered in daily dosage larger than 75 mg. given in divided doses. When cortisone is withdrawn, it should be done slowly, and administration of ACTH for several days may help to stimulate the adrenal cortex. When a patient who has received prolonged cortisone therapy is subjected to some shocking procedure (such as operation), it is important to look carefully for signs of shock associated with adrenal cortical depression. Slocumb and Lundy[1] advised that these patients be given daily intramuscular injections of 100 to 200 mg. of cortisone for two or three days preoperatively and daily postoperatively until the danger of shock is past.

HYDROCORTISONE

Hydrocortisone, also available for treatment of rheumatoid arthritis, has the same antirheumatic effect as cortisone. However, it seems unlikely that it will prove more beneficial than cortisone in such cases. Moreover, hypercorticism will result from excessive amounts of hydrocortisone.

The intra-articular injection of hydrocortisone acetate will temporarily alleviate the symptoms of many patients with rheumatoid arthritis. Unfortunately, relief lasts only a few hours or at most a few days and repeated injections do not produce any longer relief. When a patient has osteoarthritis as well as rheumatoid arthritis, the relief is more spectacular. This applies chiefly to weight bearing joints.

In some patients symptomatic osteoarthritis of knees and ankles can be considerably relieved by intra-articular injection of hydrocortisone. This agent has a unique property of overcoming pain, stiffness, and often swelling, when applied locally in 25 to 50 mg. doses. The duration of relief varies without apparent reason and may last for many months. Repeated injections seem to afford the same relief, but if symptoms recur too rapidly, repeated injections are not feasible. If the initial injection fails to afford relief, it would be advisable to repeat the procedure at least one or two times

with slightly larger doses. The knees, ankles, and interphalangeal joints offer the best sites for treatment. The hip is more difficult to inject. Care must be exercised to avoid injecting Compound F into an infected joint.

Injections of hydrocortisone into the acutely involved joints of patients with gout may alleviate the pain and swelling. This has proved of value when the usual drugs of choice were contraindicated, as in the patient with gout and an acute gastric ulcer or an intestinal lesion that could be aggravated by colchicine. The drug can also be helpful when physical therapy of an involved joint is hindered because of undue pain.

BENEMID

In the past, management of the patient with gout between acute attacks and prophylaxis of the acute attacks centered around a low purine—low fat diet, and possibly large doses of aspirin (40+ grains/day). Some therapists have gained the impression that daily doses of colchicine help prevent recurrences of acute attacks of gout. Colchicine's action is unknown but it has been evident that it lacks a uricosuric effect. In benemid we now have a drug which has a pronounced uric acid diuretic effect and it appears to be effective in reducing the chronicity, and possibly the number of acute attacks, of gout. Benemid is often mistakenly given for acute attacks and sometime it is used for two to three days then discarded. It should be prescribed with the understanding that, if tolerated, its administration should be continued until it is evident that the pattern of attacks has been altered favorably or that it has not helped.

Benemid acts through the renal tubules and it does not allow complete reabsorption of filtered urates. It must be given in daily doses of 1 to 2 gr. but if nausea develops, the dosage should be reduced. Aspirin will nullify its action. It is still necessary to treat acute attacks of gout with colchicine or one of the newer agents, even while benemid is being given.

PHENYLBUTAZONE

During the past year phenylbutazone has been available as an antirheumatic drug. It has proved helpful at least in the temporary management of rheumatoid arthritis (including rheumatoid spondylitis). Approximately 7 out of 10 patients with symptomatic rheumatoid arthritis obtain subjective relief, which in some cases means almost complete alleviation of symptoms. Why absolutely no response is obtained in some patients is not known. The manner of action is also not known, but the reduction in swelling and size of nodules, and the increase in motion suggest more than mere analgesic properties.

Because butazolidin is not innocuous, adequate precautions must be taken. Agranulocytosis has been reported in a moderate number of cases and one death has been reported following its administration. It often causes severe abdominal pain, as well as nausea and vomiting. However, if taken immediately after meals, it is less likely to cause a gastrointestinal disturbance. It should not be given to patients with gastric ulcers and may be given only with extreme caution to those with a history of an old peptic ulcer. Edema, jaundice, dermatitis, vertigo, and thrombocytopenia also have been reported following its use.

Butazolodin is administered in doses of 200 mg. after each meal. It may be given four times daily but the increase in dosage does not seem to increase the efficacy of the drug to any unusual degree. A seven to ten day trial will suffice to determine if any benefit will be obtained. If no improvement results, it seems useless to continue the medication. If improvement does occur, the aim should be to obtain the maximum benefit then reduce the daily dosage to the minimum required. Occasionally, comfort can be maintained by administration of 100 mg. three times a day. Patients who take butazolidin should be warned to reduce their salt intake, as sodium retention and edema will quickly follow administration of the drug. Therefore, its use in patients with cardiac or renal damage may be harmful. As the drug has been available only a short

period, its final value remains undetermined.

Butazolidin has also given symptomatic benefit to some patients with severe osteoarthritis. Acute gout responds favorably to butazolidin and it may prove the most effective treatment. Chronic gouty arthritis has been relieved by this agent; 100 to 600 mg. daily in divided doses is sufficient to control symptoms. This drug also has the property of lowering the serum uric acid level. If this apparent effectiveness in gout continues and toxicity does not become a greater problem, some patients may find butazolidin more helpful than colchicine.

HYALURONIDASE

One of the distressing complications of hemophilia is hemarthrosis. It now appears that injection of 1000 turbidity reducing units of hyaluronidase (mixed with a 1 per cent solution of procaine) into the acutely involved joint will relieve the pain and allow better mobility within forty-eight hours, resulting in greater salvage of joints.[2]

OTHER MEDICAL ADJUNCTS

The increasing list of antibiotics makes available additional medications to combat infectious (bacterial) arthritis. However, they are indicated only when a specific articular infection is demonstrated. Roentgen-ray treatment continues to afford relief to many patients with rheumatoid spondylitis. The muscle-relaxing drugs, such as tolserol, are helpful in some patients with muscle spasm.

CONCLUSIONS

The medical adjunctive treatment of arthritis represents only one facet in our attack on this disease. Preservation of articular function is one of the primary aims, and use of drugs without the proper rest, physical therapy, general supportive measures and other accepted basic measures has failed to produce the best results.

Aspirin and other salicylates remain valuable therapeutic agents in most types of arthritis and despite enthusiasm for newer drugs, if the same benefits can be obtained from these simple medications, they should not be discarded in favor of toxic preparations. During the last few years, though, other drugs have been shown to be of additional value in the treatment of arthritis, and their correct use will afford more relief for those patients with arthritis.

REFERENCES

1. Slocumb, C. H. and Lundy, J. S.: The use and abuse of cortisone in surgery. S. Clin. North America 32:1165 (Aug.) 1952.

2. MacAusland, W. R., Jr. and Gartland, J. J.: Treatment of acute hemophilic hemarthrosis. New England J. Med. 247:755 (Nov. 13) 1952.

DISCUSSION

Dr. Jack Wickstrom, (New Orleans): I wish to congratulate Dr. Weiss on his comprehensive, concise presentation, and wish to echo his somber words of caution as to the limitations of some of the newer steroid and other anti-rheumatic drugs. In this age of "Wonder Drugs," "Miracle" fibers and fabrics, jet planes and atomic bombs, wishful thinking has led some of us to develop a therapeutic misconcept in the problems of arthritis. The search for the "Single Pill" or injection or the magic device that can be applied by simply pushing a button that will solve the multiple problems presented in managing arthritics is intriguing but impractical.

In dealing with any clinical problem with as many varied etiological and pathological facets as arthritis presents, it should be obvious that no single therapeutic agent or device can be universally successful. However, combining proper drug therapy with a comprehensive plan of joint protection during the period of acute inflammation, followed by therapeutic exercises once the inflammatory reaction has subsided, and the prevention of further trauma to the involved joints by adequate bracing, can salvage much useful function in these joints and can rehabilitate many of these patients.

Splinting of the acutely inflamed joint in a position of function serves to prevent deformity, reduce the degree of discomfort and the necessity for large amounts of sedation. Splinting is maintained only as long as the acute inflammatory reaction is evident.

Therapeutic exercises are invaluable in breaking the vicious cycle of muscle atrophy, joint instability—pain on attempted use, followed by further inhibition of muscle tone and disuse. This is most dramatically evident in managing the osteoarthritic knee in which progressive resistance exercises by use of a weight suspended from the ankle can restore tone to the quadriceps, and by doing so, produce stability of the knee with subsequent reduction of pain in the osteoarthritic knee to the point of insignificance.

The use of braces to correct deformity is best illustrated by the adaptation of hand braces used in restoring function after severe trauma. By overcoming joint contractures and restoring muscle

balance, many severely deformed arthritic hands can be restored to a remarkable degree of usefulness. Bracing also offers much as a means of preventing joint trauma and subsequent reactivation of the arthritic process. Such protective bracing is especially beneficial in managing arthritic knees and ankles.

Cortisone and hydrocortisone appear most beneficial when utilized to diminish the severity of symptoms of pain and inflammation of the joints so that corrective therapeutic exercises can be instituted earlier and with more vigor. The local instillation of hydrocortisone into osteoarthritic and post-traumatic arthritic knee joints has been most encouraging in this respect.

Butazolidin has proved exceptionally beneficial in the same respect of alleviation of acute joint symptoms to allow restoration of joint motion by early exercises. This has been especially true in adhesive peri-capsulitis.

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DIAGNOSIS OF DIABETES

This year, November 15 to November 21, is Diabetes Week. Special attention will be directed during this week to finding the unknown diabetic. The campaign has been inspired and organized by the American Diabetes Association and accomplished through the combined efforts of the Association with the State and county medical societies. Local programs are sponsored and conducted directly by the local societies. In previous years it has been felt that probably for every diabetic under treatment there is one that is yet undetected. When this diabetes is recognized and control instituted, the better chance there will be to avoid deteriorations.

While diabetes is one of the few important diseases in which laboratory procedures are necessary for intelligent management, careful clinical examination is essential for diagnosis. Only by such means can the proper classification be done and adequate laboratory procedures carried out. At this point it is necessary to emphasize again that the absence of sugar in the urine and a normal blood sugar do not eliminate diabetes. On the basis of experience, the American Diabetes Association has adopted standards which can be considered the upper limit of normal for blood sugar. Using venous blood in the Folin and Wu method, a blood sugar fasting of over 130, or after eating over 200, diabetes is regarded as present. However, Joslin makes the statement that "patients with glycosuria whose venous blood sugar is 130 mg. per 100 cc. fasting, or 170 mg. per 100 cc. at any other time of day, are diagnosed as diabetics." With capillary blood sugar determinations used in the Folin-Malmros method the figures are slightly higher.

In many instances in which clinical examination is suggestive but blood sugar determinations are inconclusive, glucose tolerance tests, possibly repeated, become essential. Also, in some patients without symptoms and with glycosuria, glucose tolerance tests are also necessary. At this point the matter for the clinician to decide is which glucose tolerance test and what is its interpretation. Womack and Moyer[1] have reported on the evaluation of four types of glucose tolerance tests in a heterogeneous group of 71 patients with glycosuria and without symptoms. The tests were the four commonly used, which were the three hour, one dose ("standard") oral test, the one hour two dose (Exton-Rose) test, the intravenous test, and the two hour postprandial blood sugar level. They found significant disagreements in the interpretations of these tests as pertaining to individual patients. They found that fasting blood sugar levels, per se, were unreliable criteria for determining the presence or ab-

sence of diabetes mellitus, and similar disturbances of carbohydrate metabolism. They also reported that although the intravenous tolerance test was somewhat less sensitive than the standard oral test, both were considered satisfactory as clinical tests in suspected cases of diabetes mellitus. They considered the postprandial blood sugar determination compared well enough with the standard test to be of value as a presumptive test for diabetes. The one hour, two dose, oral (Exton-Rose) test they considered as excessively sensitive and unreliable and should be discarded as a diagnostic laboratory procedure. They found, additionally, that the correlation between the degree of glycosuria and the severity of disturbance of glucose tolerance in this group of patients was poor. On the basis of the standard test among these 71 patients with glycosuria, 21 were found to be diabetic, 15 presumably diabetic, and 35 normal.

Soskin[2] has advocated adherence to the intravenous glucose tolerance test on the basis of clinical considerations and the results obtained in experimental animals. He considers that the glucose tolerance test is chiefly an index of the efficiency of the blood sugar regulation by the liver under the influence of various endocrine glands, in which the hormones from the pancreas are among others that are contributory. He feels that the variability of absorption from the intestinal tract when glucose is given by the oral route is such as to make the test under these conditions practically worthless.

To further clarify a situation when even a glucose tolerance test is inconclusive, Berger[3] advised administration of 100 mg. of corticotropin prior to the standard glucose tolerance test. The test was carried out on known diabetics, siblings of known diabetics, and controls. In 12 known diabetics, after corticotropin, the curve was approximately 30 per cent higher at two hours than without corticotropin. Among 14 siblings, the blood sugar at two hours averaged 200 before, and 280 after the administration of corticotropin. In 38 controls, there were two instances in which the use of corticotropin was followed by a rise in the blood sugar curve which was regarded as significant. The author suggests that this study may improve the sensitivity of the glucose tolerance test but that appropriate follow-ups of from five to ten years will be necessary to prove it.

Best has stated recently that a lack of insulin produces a failure of fat, protein, and carbohydrate formation and storage, a decreased oxidation of sugar and derangement of phosphate and potassium metabolism, with a loss of these substances, as well as sugar, nitrogen, and ketones, from the body.

With these considerations in mind, the physician can approach the problem of diagnosis of diabetes with gravity. He should feel that the problem is one susceptible of solution if given sufficient time and cooperation.

1. Womack, C. R., and Moyer, J. H.: Practitioner 3:479, 1952.
2. Soskin, Samuel: Postgraduate Med. 10:108 (August) 1951.
3. Berger, Herbert: J. A. M. A. 148:364 (Feb. 2) 1952.

ORGANIZATION SECTION

The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.

An informed profession should be a wise one.

1954 ANNUAL MEETING

The 1954 Meeting of the Louisiana State Medical Society will be held in New Orleans on May 20, 21, and 22 (Thursday, Friday, and Saturday) with headquarters at the Roosevelt Hotel.

After discussion with members of the Society in various sections of the State, it was concluded that it was not possible to obtain suitable accommodations for this meeting outside of the City of New Orleans. The Orleans Parish Medical Society, as a conse-

quence of this, has agreed to again be host to the Society in 1954 and plans are now under way for arrangements in connection with the meeting.

Although there has been considerable delay in initiating these plans, with the cooperation of the doctors of New Orleans, the Roosevelt Hotel and the Chamber of Commerce, a good meeting is anticipated. Further data concerning the meeting will be published when this is available.

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TOO LITTLE, TOO LATE

When the House of Delegates approved and adopted our group plan of accident and health insurance, the Continental Casualty Company of Chicago, one of the oldest and most reliable companies writing this kind of insurance today, agreed to accept *all* applicants regardless of disability and without a doctor's examination, provided 50% of our members enrolled during the Charter Enrollment Period.

For one reason or another 75% of our members waited for 50% to apply. You procrastinated too long. The enrollment period has ended; consequently the company had to refuse coverage to the uninsurable doctors.

You are reminded, however, that you may still enroll at any time *if* you are in good health. You should submit your application, because this is your plan. It is sponsored by your Society, for your benefit. It needs your support and you need its protection. You will receive better service if you are insured by a company sponsored by your Society, and where you can take up any claims or other matters locally, because all claims will be paid by Emery & Kaufman, 314 Camp Street, New Orleans, Louisiana State Administrators for the Continental Casualty Company.

If enough interest is shown by our members, during the next few months, we will request the Company to allow us the privilege of another open enrollment period, during which time they will again accept application from the uninsurable members and issue policies to them, if a sufficient number of our members enroll to bring the total number up to 50 per cent of the total membership in our Society. Since the Company has agreed to include the number of members already enrolled in the Orleans Parish Medical Society group as part of the required 50 per cent, it should not be too har a task to secure the percentage requested of us, and this should be our inducement to all members—the insurable as well as the unsurable—to enroll at once.

Many of our fellow members cannot get this insurance or any other insurance, without being rated up or submitting to some waiver provision, unless they secure same through our group policy, and then only during an open enrollment period. If the members who have no disability would enroll, it would help our less fortunate members to protect themselves and their families, and would no doubt encourage the Company to give them another chance at an open enrollment period. Won't you enroll now while you can? Tomorrow may be too late.

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WORTHWHILE SUGGESTION

Your Secretary attended a most interesting and enthusiastic meeting of a joint session of the Evangeline Parish and Avoyelles Parish Medical Societies on October seventh at Ville Platte, where he among other members and legislator guests discussed the question of chiropractic as it affects our State and the Nation. It was a very instructive meeting from many points of view, creating quite a bit of interest and enthusiasm and establishing methods of contacting our legislators in our fight against these cultists at our next legislative session.

We believe that more meetings of this nature should be held by our component parish societies, inviting the respective legislators of these parishes to the meetings. Much can be accomplished in educating these legislators as well as some doctors as to what chiropractic would mean to our State if they were legalized to practice here.

After the legislature is in session, it will be too late to meet and defeat this attack

upon our profession and especially to protect our people from the damaging effects of allowing these cultists to practice in our State. We should begin our campaign now to pledge our legislators to vote against any bill they might have introduced to legalize themselves to practice in Louisiana.

You know that these chiropractors are working and have been active since the last session of the legislature.

Don't let us be caught with our "pants down." Why not get busy and help us give these cultists the worse beating they have ever received?

We would not suggest or be in favor of changing our Medical Practice Act. This Act has been upheld by not only the Supreme Court of Louisiana but also by the Supreme Court of the United States, and in every case where it has been appealed to these Courts, the decision has always been in favor of the State Board of Medical Examiners, and against the Chiropractor. This, we think, speaks well for our law, and too, quite a few of the states have copied our Act, and the practice of medicine in these respective States is controlled by it today.

Of course, the Chiropractors, first of all, would like to have their separate Board, and the next best thing they would like would be to have our Act amended.

If every member of our Society does his or her duty in this fight, we can defeat their efforts to be legalized to practice their cult in Louisiana and keep our Medical Practice Act as it is at the present time.

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LOUISIANA ACADEMY OF GENERAL PRACTICE

The Louisiana Academy of General Practice held its Annual Convention at the Bentley Hotel, Alexandria, on September 21-23, and to say it was a very enjoyable and instructive meeting would be putting it rather mildly. There was a good attendance and the members of the faculty of the University of Tennessee presented the practitioners with a very instructive program which was enjoyed by all present.

It was my pleasure to attend this meeting with Dr. Philip H. Jones, our President, and it goes without saying that we enjoyed not only the scientific treat offered but the many courtesies shown us and the delightful social functions planned for the enjoyment of its members and guests.

The following officers were elected for 1953-1954:

President—Dr. John W. Atkinson, Gretna, La.

President-elect—Dr. Janie Topp, Lake Charles, La.

Secretary—Dr. Esmond A. Fatter, New Orleans, La.

1st Vice President—Dr. Vincent P. Blandino, New Orleans, La.

2nd Vice President—Dr. W. A. McBride, Shreveport, La.

Treasurer—Dr. Edwin R. Guidry, New Orleans, La.

Past President—Dr. E. L. Carroll, Columbia, La.

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THE ST. LOUIS CLINICAL SESSION

If the members of our Society expect to attend the Seventh Annual Clinical Session of the American Medical Association December 1-4 in St. Louis, it is time to make hotel and traveling reservations. Judging from the program prepared for this year, we might expect an unusually interesting meeting, covering many and varied topics, furnishing a post-graduate course in medicine and surgery.

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INTERESTING OBSERVATION

Does the following sound like we have a shortage of doctors in this country? Many of the people who are claiming a shortage of doctors exists, often do so to create the impression that the American people are suffering from the want of good medical care, and as a remedy, they would and do advocate government medicine, which we all know would give us political medical services, inferior in character, and wholly unacceptable to the American people. The citizens of this nation still believe in the free-enterprise system of medicine and demand the preservation of that most precious personal relationship between doctor and

patient, and will not be satisfied with less.

"TWICE AS MANY interns and resident physicians today are completing their training and furthering their education through hospital work as there were prior to World War II. During 1952-1953, there were 7,645 interns and 16,867 resident physicians on duty in the nation's hospitals, compared to a total of approximately 12,000 in 1940."

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FACTS WORTH KNOWING

The term of years during which there is a legal obligation to pay debts varies from two years in Texas to eight years in Wyoming. Legal action to collect a bill must be taken within the statutory period or the debt is outlawed and a physician, for example, cannot recover at law from the patient.

The following is a resumé of the statutory periods in the forty-eight states and the District of Columbia taken from a recent issue of Medical Economics:

2 years: Texas.

3 years: Alabama, Arizona, Arkansas, Delaware, District of Columbia, Florida, Kansas, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, Virginia, and Washington.

4 years: California, Georgia, Idaho, Nebraska, Nevada, New Mexico, and Utah.

5 years: Illinois, Iowa, Kentucky, Missouri, Montana, West Virginia.

6 years: Colorado, Connecticut, Indiana, Maine, Massachusetts, Michigan, Minnesota, New Hampshire, New Jersey, New York, North Dakota, Ohio, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Tennessee, Vermont, Wisconsin.

8 years: Wyoming.

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LOUISIANA STATE MEDICAL SOCIETY NEWS

CALENDAR

PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Tuesday of every month	Baton Rouge
Morehouse	Third Thursday of every month	Bastrop
Natchitoches	Second Tuesday of every month	
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

DR. JAMES ALLEN ELECTED CHAIRMAN OF THE NATIONAL COMMITTEE FOR RESEARCH IN EYE DISEASES AND DISABILITIES

Dr. James Allen, Professor of Ophthalmology, Tulane University, New Orleans, has been elected chairman of the newly formed National Committee for Research in Eye Diseases and Disabilities, an organization opening a new era in the nation's effort to reduce the alarming number of persons handicapped through eye disorders. The new "solid front" affiliation of medical and rehabilitation authorities was formed during the meeting in Chicago of the American Academy of Ophthalmology and Otolaryngology.

Recognition many months ago of a growing need for closer cooperation brought together representatives of professional and lay groups, including all established and accredited organizations of national scope.

"Too long have eye physicians had insufficient understanding of the total problem of the visually handicapped; and those concerned with education and rehabilitation have failed to help in promoting research to prevent eye disabilities," declared Dr. Allen when accepting his new position.

Applauding what he termed, "a significant promise of concerted action," Committee Secretary, Dr. Lorand V. Johnson, Professor of Ophthalmology, Western Reserve University, Cleveland, summarized the airs of the group as including: assessment of research and training needs, encouragement and assistance to medical schools, national referral activities, promotion of cooperation between professional and lay groups, and such special research as cannot be effectively solved by any single member agency.

Other officers in addition to Dr. Allen and Dr. Johnson are: Dr. V. Everett Kinsey, Professor of Ophthalmic Research, Wayne University, Detroit, and Director of Ophthalmic Research, Kresge Eye Institute, Detroit, first vice-president; M. Robert

Barnett, Executive Director of the American Foundation for the Blind, New York, second vice-president; Dr. Franklin Foote, Executive Director of the National Society for the Prevention of Blindness, New York, treasurer.

TWO NEW DEPARTMENT HEADS NAMED AT LSU

Two new department heads have been named to fill vacancies at the Louisiana State University School of Medicine, it has been announced by President Troy H. Middleton.

Dr. Hugh Thompson Beacham, former clinical associate professor and a member of the L. S. U School of Medicine faculty since 1931, was named professor and head of the department of urology. Dr. C. Barrett Kennedy, former clinical associate professor of dermatology, was named professor and head of the department of dermatology.

Dr. Beacham has been an instructor, assistant professor and clinical assistant professor at the L. S. U. School of Medicine. Prior to this he was a clinical assistant at Tulane University. He has also been a senior visiting surgeon in the Charity Hospital urology division.

Dr. Beacham replaces Dr. P. Jorda Kahle who retired recently. The new department head is a native of Summit, Miss., received a B. S. degree from the University of Mississippi and M. D. and M. S. degrees from Tulane.

Dr. Kennedy replaces the late Dr. James K. Howles as head of the department of dermatology. Serving L. S. U. since 1934, Dr. Kennedy received his M. D. degree from the Tulane Medical School in 1932 and interned at Charity Hospital.

TUBERCULOSIS CONFERENCE

Dr. C. M. Sharp, Jacksonville, Florida, was elected president of the Southern Tuberculosis Conference for 1954 by the delegates attending the 1953 Conference held in New Orleans at the Jung Hotel on October 1st, 2nd, and 3rd.

Miss Marietta Rocquet, executive secretary of the Tuberculosis Association of New Orleans, was elected vice-president, and Bryan Wilson of Memphis, secretary-treasurer.

The Southern Trudeau Society, medical section of the tuberculosis association, elected officers with Dr. P. M. Huggin of Knoxville as president; Dr. Sydney Jacobs of New Orleans as vice-president; and Dr. Robert K. Oliver of Montgomery, Ala., as secretary.

Named to the Executive Council of the Southern TB Conference organization where Julian Sipple of Savannah, Ga.; Thomas Debeney of Charleston, W. Va.; Dr. Huggin; and K. W. Grimley of Birmingham, Ala., and out-going president of the Conference.

Over 400 tuberculosis association workers and TB doctors attended the 39th annnual event being held in New Orleans for the first time. Outstanding speakers from the Veteran's Administration, the National Tuberculosis Association, the American Trudeau Society, and from England appeared on the three day program.

The Conference will be held next fall in Asheville, N. C.

AAGP PLANS ANNUAL ASSEMBLY IN CLEVELAND

The American Academy of General Practice makes the first official announcement of its Sixth Annual Scientific Assembly which will be held March 22-25, 1954 in Public Auditorium, Cleveland, Ohio, by disclosing the names of such top-flight men as Sir Alexander Fleming, Dr. Howard Rusk, and Dr. E. J. McCormick who are headlining the scientific program.

The entire program will be presented by men of equal note and by leaders in the fields to be covered. Family doctors who have already heard of the meeting, term it the most significant and interesting yet presented by the Academy. The program itself will be fast-paced, well diversified, and completely applicable to daily practice.

The Committee on Scientific Assembly, headed by Dr. John Mosher of Coeymans, N. Y., promises that these four days will unquestionably be the most pleasant, as well as the most instructive, doctors have ever spent at a medical meeting.

A quick look at the program shows symposia on peptic ulcer, tuberculosis, headache and dizziness, and antibiotics, a live clinic on rehabilitation procedures, presentations on the commonly missed diagnoses of skin diseases, the almost forgotten woman—the routine multipara, and unnecessary gynecologic surgery. Arthritis, anemia, surgical problems and recent advances in therapeutics will also be covered.

To supplement the formal lecture program, the Committee is putting together a scientific exhibit section of equal distinction and interest. The list is still in process of selection, but it will include more than 60 exhibits. At least half of them will be original, making their debut at this meeting. All of them will be closely integrated with the lecture program.

A full social program is being planned for the wives culminating with a President's Reception, the first the Academy has had, for the entire attendance.

MIDWINTER SEMINAR IN OPHTHALMOLOGY AND OTOLARYNGOLOGY

The eighth annual University of Florida Midwinter Seminar in Ophthalmology and Otolaryngology will be held at the Sans Souci Hotel in Miami Beach the Week of January 18, 1954. The lectures on Ophthalmology will be presented on January 18, 19 and 20, and those on Otolaryngology on January 21, 22 and 23. A midweek feature will be the Midwinter Convention of the Florida

Society of Ophthalmology and Otolaryngology on Wednesday afternoon, January 20, to which all registrants are invited. The registrants and their wives may also attend the informal banquet at 8 p. m. on Wednesday. The Seminar schedule permits ample time for recreation.

The Seminar lectures on Ophthalmology this year are Dr. W. B. Anderson, Durham, N. C.; Dr. W. P. Beetham, Boston; Dr. W. C. Owens, Baltimore; Dr. A. B. Rees and Dr. M. C. Wheeler, both of New York City. Those lecturing on Otolaryngology are Dr. E. N. Broyles, Baltimore; Dr. H. P. House, Los Angeles; Dr. W. M. McNally, Montreal, Canada; Dr. Dorothy Wolff and Dr. D. Woodman, New York City.

POST-GRADUATE TEACHING FUND FOR GIFT SUBSCRIPTIONS TO HOSPITALS

The International Academy of Proctology announces the establishment of a post-graduate teaching fun to provide gift subscriptions to the American Journal of Proctology to 750 of the largest Hospital Libraries in this country and abroad. Inasmuch as the American Journal of Proctology is the only official Proctologic Journal in the world, these subscriptions will provide a continuing post-graduate course for interns, residents and hospital attending staffs in all major hospitals.

As a teaching and educational organization, the Academy is pre-eminent in Proctology. The Annual Conventions are literally post-graduate courses, and the Journal has raised the level of Proctology throughout the world.

The International Academy of Proctology recently announced the establishment of a Research Fellowship in Proctology with a grant of $1200.00 to the Jersey City Medical Center, Jersey City, New Jersey.

1954 IODINE RESEARCH AWARD NOMINATIONS REQUESTED

Nominations are now being received by the American Pharmaceutical Association for the 1954 Chilean Iodine Educational Bureau Award recognizing outstanding research in the chemistry and pharmacy of iodine and its compounds as applied in pharmacy or medicine.

The award consists of $1,000 and a diploma setting forth the reasons for selection of the recipient. It may be presented each year at the annual meeting of the Association.

Any member of the Association may propose a nominee by submitting eight copies of each of the publications to be considered in the competition, a biographical sketch of the nominee including date of birth, and a list of his publications. Eight copies of the nomination must be submitted to Robert P. Fischelis, Secretary of the American Pharmaceutical Association, 2215 Constitution Ave., N. W., Washington 7, D. C. To be eligible for the 1954 Award, nominations must be received on or before January 1, 1954.

A nominee must be a resident of the United States or Canada. He must have accomplished outstanding research in the chemistry or pharmacy of iodine and its compounds as applied in pharmacy or medicine.

During the period covered by the nomination the nominee shall have been actively engaged in, shall have completed, or shall have published a report upon the line of investigation for which the award is made. During the period of two years prior to the date of nomination, the nominee shall not have been engaged in research under the sponsorship of the Chilean Iodine Educational Bureau, Inc.

The recipient will be selected by an award committee which is appointed by the chairman of the Association's Council. The present committee includes Justin L. Powers, chairman; Paul Block, Louis Gershenfeld, Harvey B. Haag, Lloyd M. Parks, Heber W. Youngken, and Charles O. Wilson.

The recipient will deliver a paper or lecture upon the subject of his scientific work at the meeting at which the award is conferred. His paper, or address, will then be published in the Journal of the American Pharmaceutical Association. Travel expense to the meeting at which the award is to be made is provided for up to $250.

CONFERENCE ON CARE OF THE LONG-TERM PATIENT

Grants totalling $35,000 to provide for the national Conference on Care of the Long-Term Patient, to be held in Chicago, March 18-20, 1954, have been made by the Rockefeller Foundation, the Liberty Mutual Insurance Company, the New York Life Insurance Company, the Metropolitan Life Insurance Company, and the Equitable Life Assurance Society. Approximately half of the funds needed are required for the preparatory or pre-Conference phase and have been made available by the Foundation. The other half—for the Conference meeting—has been provided by the insurance companies.

The American Hospital Association, the American Medical Association, the American Public Health Association, the American Public Welfare Association, and the U. S. Public Health Service are serving as sponsors and supplying staff for the Conference, which has been envisioned as the logical sequel to the previous National Conference on the Preventive Aspects of Chronic Illness which was held in Chicago in March of 1951. The Commission on Chronic Illness is serving as the planning committee for the 1954 Conference.

BECTON, DICKINSON INTRODUCES NEW INTERCHANGEABLE SYRINGE

Becton, Dickinson and Company has announced

the introduction of "BD Multifit," a new syringe that provides the convenience and economy of interchangeable parts, the performance of an individually fitted syringe and the durability of a clear glass molded barrel.

A leader in the syringe field since 1898, when it first began to produce the then revolutionary Luer all-glass syringe, the company revealed that Multifit has been achieved after many years of research and development of special equipment.

Multifit syringes are being introduced in 2 cc. and 5 cc. sizes. Later the company plans to introduce additional sizes.

Performance of the new interchangeable syringe has been tested for two years in metropolitan hospitals. In every case, exceptional savings in time and equipment were reported. Back-flow and jamming were virtually eliminated. Nurses were able quickly to reassemble, handle and clean the equipment.

Multifit syringes apply the Becton, Dickinson and Company principle of unground, molded clear glass barrels to preserve the protective "skin" of the glass and thus to ensure maximum durability.

DRAMATIC RESULTS WITH ISUPREL CITED IN TREATING EMPHYSEMA

Use of Isuprel, a sympathomimetic aerosol, has produced "very dramatic relief following a few inhalations" in patients experiencing bronchiolar spasm accompanying emphysema, according to Dr. Louis L. Friedman, Birmingham, Ia.

Writing in the Journal of the Medical Association of the State of Alabama (22:255, April 1953), he calls the ultimate prognosis in emphysema "poor" but adds that Isuprel and similar drugs are indicated in relieving spasm. Regular and routine use of Isuprel is frequently necessary.

Dr. Friedman recommends use of a barbiturate, bromide or any satisfactory sedative in acute attacks of dyspnea to relieve the apprehension of the patient. Anxiety tends to aggravate all of the clinical symptoms, especially dyspnea, he notes.

SURGICAL ASSOCIATION OF LOUISIANA

The Surgical Association of Louisiana will hold its Sixth Annual Meeting on Sunday, November 15, at the St. Charles Hotel, New Orleans, Louisiana, at which time the following scientific program will be presented:

Abdomino-perineal Resection of the Colon and Rectum, by Dr. Charles H. Mosely, Attending Surgeon, Lady of the Lake Hospital and Baton Rouge General Hospital, Baton Rouge, Louisiana.

The Complications of Colostomy, by Dr. Lawrence J. O'Neil, Chief, Independent Surgical Service, Charity Hospital, New Orleans, Louisiana.

Care of the Injured Hand, by Dr. Michael L. Mason, Professor of Surgery, Northwestern University, Attending Surgeon, Passavant Memorial Hospital, Chicago, Illinois.

Benign Breast Lesions, by Dr. Samuel Karlin, Assistant Professor of Surgery, Louisiana State University Medical School; Sr. Surgeon, Touro Infirmary; Sr. Visiting Surgeon, Charity Hospital, New Orleans, Louisiana.

Benign Pancreatic Disease, by Dr. Charles B. Puestow, Clinical Professor of Surgery, University of Illinois College of Medicine; Chief, of Surgery, Henroten Hospital, Chicago, Illinois; Chief, Surgical Service, Veterans Administration Hospital, Hines, Illinois.

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BOOK REVIEWS

Sterility: Its Cause and Treatment; by J. Jay Rommer, Springfield, Ill., Charles C Thomas, 1952, pp. 427, Illus. Price $12.50.

This book on sterility by Dr. Jay Rommer has a very large assortment of facts and theories pertaining to the barren couple. However, the book is poorly organized in that there is no systematic approach to the study of a sterile couple. Much more important, is the fact that there is no effort made to differentiate the important from the unimportant details. Too much space is given to the trivia and not enough to the significant aspects of a sterility work-up.

For the modern gynecologist interested in sterility this book offers nothing new. For the general practitioner working to improve his knowledge of the cause and treatment of sterility, only confusion is offered.

Entirely too much emphasis is placed on the pelvic pathology produced and the necessity for surgical correction of the retrodisplaced uterus. There are still some legitimate reasons for suspension of the uterus, but these are few and far between.

Also a statement is made that malignant degeneration occurs in about five per cent of fibroids. This was obtained from a reference printed in 1906. In 1952, when this book was published,

most authorities in this country placed the figure at less than one per cent.

All in all, in too many important aspects, this book is way out of date.

M. DURALDE CLAIBORNE, M. D.

Battle Casualties; by Gilbert W. Beebe, Ph. D. and Michael E. De Bakey, M. D. Springfield, Ill., Charles C Thomas, Publisher, 1952. pp. 277, illus. Price $10.50.

In *Battle Casualties* the authors have collated data of the Army Medical Service of World War II in order to aid in the planning and evaluation of surgical care for the wounded in modern warfare. The book is primarily of interest to the military surgeon; however, the opinions expressed are those of the authors and not of the Army.

This volume will prove af great interest to the men being called into the medical services at the present time. The civilian surgeon can obtain much valuable information about the purposes and problems of the military surgeon as well as about planning necessary for civilian defense.

The most impressive aspect of the volume is the tremendous amount of data which has been sifted and rendered into graphs and tables. It is useful for teaching and for obtaining data for comparison with hospital statistics.

PAUL TRAUTMAN, M. D.

A Textbook of Clinical Neurology; with an Introduction to the History of Neurology; by Israel S. Wechsler, M. D. 7th ed. Philadelphia, W. B. Saunders, 1952. Pp. 801, illus. Price $9.50.

The seventh edition of this text remains the reference of choice for practitioners in the fields of medicine other than Neurology as well as a ready reference text for the practising neurologist. As pointed out in the preface to this edition, the subject of treatment of infectious diseases of the nervous system has been revised. In addition newer concepts in neurology, developed since 1947, the date of the last edition of this text, have been included.

The clear and concise approach to neurological examination found in the previous editions of this work is retained. The section on psychological diagnosis though brief, is overly compensated for by the dynamic approach to the neuroses found in the latter part of the text. The concluding introduction to the history of neurology completes a text which should be of invaluable use to the practising clinician.

T. BLOCH, M. D.

PUBLICATIONS RECEIVED

Winfred Funk, Inc., N. Y.: Cure Your Nerves Yourself, by Louis E. Bisch, M. D.

Lea & Febiger, Phila.: A Primer of Cardiology, by George E. Burch, M. D. (2nd Edit.); Spatial Vectorcardiography, by George E. Burch, M. D., J. A. Abildskov, M. D., and James A. Cronvich, M. S.

Health Education Council, N. Y.: Films in Psychiatry, Psychology & Mental Health, by Adolf Nichtenhauser, M. D., Marie L. Coleman and David S. Ruhe, M. D.

Medical Library Co., N. Y.: Respiratory Diseases and Allergy, by J. S. Smul, M. D.

North Castle Books, Greenwich, Conn.: It's NOT ALL In Your Mind, by H. J. Barglund, M. D., and H. L. Nichols, Jr.

Charles C Thomas, Springfield, Ill.: A Source-Book of Medical Terms, by Edmund C. Jaeger, D.Sc.; Regional Block, by Daniel C. Moore, M. D.